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16th European Symposium on Organic Chemistry (ESOC 16), Prague, Czech Republic

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The 16th installment of the increasingly popular European Symposium on Organic Chemistry was held in Prague, Czech Republic, from July 12–16, 2009. The highly successful meeting was organized by the Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic, under the chairmanship of *Ivo Starý* in the beautiful Municipal House of Prague. The multitalented Ivo Starý showed that as well as being a successful organic chemist he is also a talented musician, joining in the opening ceremony in the grand Smetana's Hall, playing Bach's piano concerto in F minor with his fellow musicians (Figure 1). The week saw some outstanding contributions not only from Europe, but also from further afield, with broad-ranging research highlighting the diversity for which the ESOC meeting has become renowned.

Figure 1. Orchestra playing Bach's piano concerto at the opening ceremony of the symposium. The Chairman of the symposium, Ivo Starý, is pictured second from the right.

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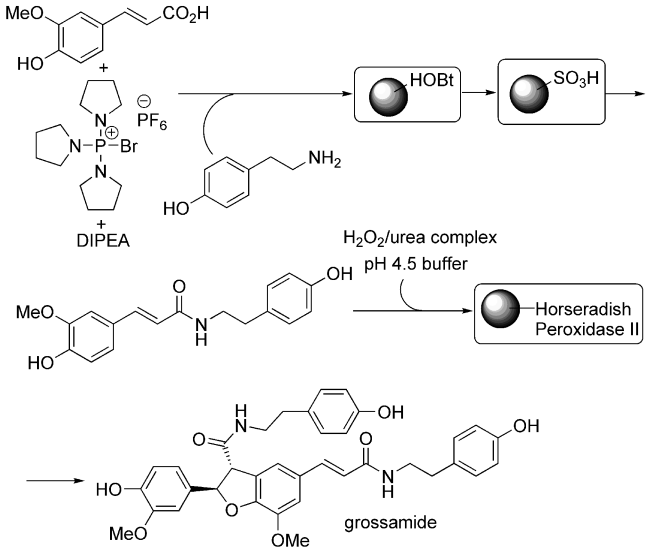
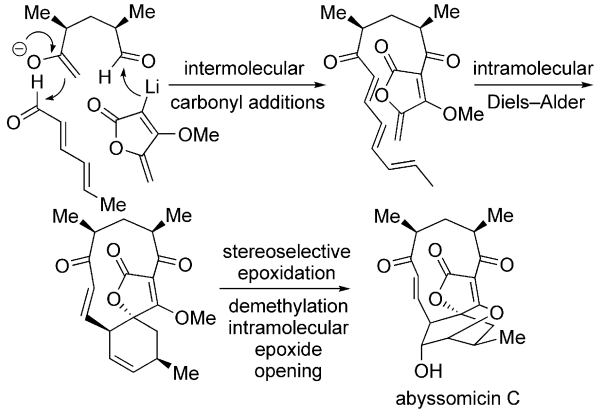
Flow chemistry is developing into an extremely powerful tool in catalysis and organic synthesis. This was demonstrated in an emphatic fashion by *Steven Ley* (University of Cambridge, UK) in his keynote lecture. With an ethos of "relegating routine steps to machinery" he showed how his group could in principle perform up to a thousand experiments a day by using modular flow chemistry equipment, eliminating the need for time-consuming steps, such as chromatography, washes and crystallizations. Reactions can be controlled remotely at any time over the internet, and they also benefit from increased efficiency and reactivity (e.g., Wittig reactions complete within 1 s), much lower solvent usage, enhanced safety, on-demand synthesis and telescoped reaction sequences. Reactants are pumped into the flow phase and react on microfluidic chips. Further modifications to reactions, such as catalysts, extra reagents, scavengers and catch-and-release systems can be introduced into the system through solid-phase column modules. The products from the flow chemistry can be output to microfluidic devices containing biological targets of interest, and any "hits" can be rapidly screened. The Ley group has performed a diverse array of organic chemistry employing these flow systems, including the syntheses of 4,5-oxazoles, fluorination of aldehydes and alcohols, fluoro-Ritter reactions, "click" chemistry, Seyferth–Gilbert acetylene synthesis, pyrazole synthesis and Heck reactions. This flow methodology has also been applied impressively to the synthesis of natural products such as oxomaritidine, *O*-methyl siphonazole and grossamide (Scheme 1).

Using more conventional laboratory techniques, *Eric Sorensen* (Princeton University, USA; Figure 2) illustrated beautifully how natural product synthesis can be guided by the concept of architectural self-construction. Sorensen began by discussing several landmark syntheses, showing how



Scheme 1.

the concept of using ideas about the biogenesis of natural compounds has emerged as a powerful tool in synthetic molecular construction, citing *Sir Robert Robinson's* pioneering synthesis of tropinone as the probable foundation of biomimetic synthesis. Guided by proposals in the biosynthesis of hexacyclinic acid from ^{13}C-acetate feeding experiments, an efficient enantioselective synthesis of the potent microtubule-stabilizing agent FR182877 was designed, starting from a linear polyunsaturated compound. The key step involved a previously unknown double transannular Diels–Alder reaction, creating a 19-membered macrocyclic pentaene, generating 7 stereogenic centres with complete diastereocontrol. The synthesis could be performed on a multigram scale, giving an overall yield of between 5 and 6% over 20 linear steps. A highly diastereoselective Diels–Alder macrocyclization was also utilized in the asymmetric synthesis of the antibacterial natural product (–)-abyssomicin C. The strategy relied on three-component intermolecular carbonyl additions, an intramolecular Diels–Alder reaction, epoxidation and finally epoxide ring opening (Scheme 2). The synthesis was achieved in 15 steps, and significant amounts of the compound were made for biological evaluation. It is thought that the electrophilic enone system reacts readily with nucleophiles. The Diels–Alder reaction was again central to the synthesis of the tricyclic β-keto ester core of hirsutellone B, known to exhibit antimicrobial activity against *M. tuberculosis*. A retro-Diels–Alder fragmentation of a 2,2-dimethyl-1,3-dioxinone heterocyclic intermediate formed a transient acyl ketene that rapidly underwent both lactam formation and intramolecular Diels–Alder cyclization. The highly diastereoselective synthesis gave a 6% yield over 13 steps.



Scheme 2.

Continuing along the natural product synthesis theme, *Martin Kotora* (Charles University, Czech Republic; Figure 2) demonstrated versatile zirconium-mediated cyclization and alkylation reactions for the synthesis of the steroid estrone. Starting from a substituted styrene derivative, Cp_2ZrBu_2 (Negishi's reagent) promoted alkylation with 3,4-dichlorobutene and subsequent cyclization, installing the A and B rings of the steroidal scaffold. The next alkylation–cyclization sequence with 2,3-dichloropropene proved unsuccessful due to a competing oxidative addition into the C–Cl bond. This problem was circumvented by using the corresponding 2-fluoro-1,7-diene, where oxidative addition into the C–F bond did not occur. The final cyclization was performed by using ring-closing metathesis to furnish the estrone scaffold in a total of nine steps. A second-generation, more efficient synthesis was conducted in an overall 50% yield by using Pauson–Khand methodology for the final ring closure. This method was extended into the enantioselective synthesis, for which the zirconocene was not compatible, giving the desired compound in greater than 98%*ee*.

Redesigning natural products to improve their efficacy as potential anticancer agents was the subject of the lecture by *Sergey Kozmin* (University of Chicago, USA). He stressed the urgent need for new chemotherapeutic agents designed to target cancer progression. Bistramide A, known to selectively activate protein kinase C (PKC) isotype δ, leading to growth arrest in cancer cell lines, was cleverly stitched together by using a key three-component cross-metathesis reaction. The flexibility of the methodology allowed for a number of synthetic analogues to be made and tested for structure–activity relationships. A potent and reversible actin modulator was rationally designed, lacking the enone moiety present in bistramide A, giving reduced toxicity. A

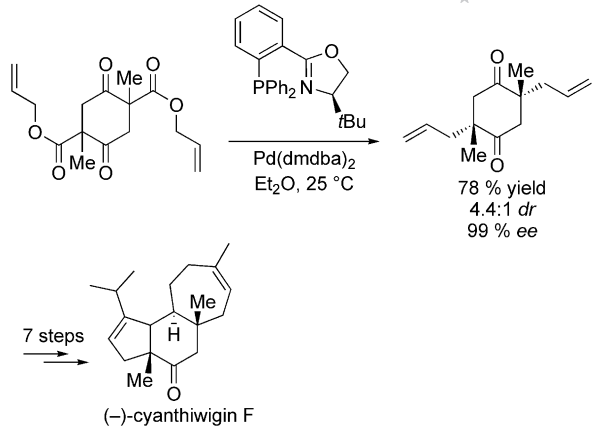
Figure 2. Eric Sorensen (left) and Martin Kotora (right) explaining their chemistry to the audience.

number of other compounds were also developed for targeting glycolytic metabolism, which is up-regulated in cancerous cells.

Joëlle Prunet (École Polytechnique, France) discussed an innovative synthesis of the powerful antitumour agent Taxol by using a challenging metathesis-based approach. After the first-generation convergent synthesis proved to be unsuccessful, a second-generation, semiconvergent synthesis was designed. The strategy relied upon a Shapiro reaction, ring-closing metathesis and an aldol condensation as the key steps. Interestingly, the outcome of the ring-closing metathesis reaction to install the eight-membered B ring was influenced by the diol protecting group at the C-1 and C-2 positions. Acetonide derivatives gave only cross metathesis products upon treatment with Grubb's second generation catalyst, with the head-to-head dimer predominating. Both the corresponding benzoate derivative and the free diol gave a quantitative yield of the desired eight-membered ring.

Brian Stoltz (California Institute of Technology, USA) gave an inspiring synopsis of how natural products are the driving force of reaction development within his research group. Target-directed synthesis frequently requires new reaction methodology that can often instigate the synthesis of novel targets. This was exemplified in the first example of a catalytic enantioselective allylation of enol carbonates and silyl enol ethers, by using various allyl carbonates, a Pd^0 catalyst and a chiral phosphanyloxazoline ligand, for the formation of all carbon quaternary centres. A ligand screen revealed that (*S*)-*t*Bu-phox in combination with $Pd_2(dba)_3$ (2.5 mol-%) gave the best results in this enantioselective Tsuji allylation. This methodology was then applied to the first enantioselective synthesis of (–)-dichroanone in an overall yield of 4% over 11 steps, without the use of protecting groups. The synthesis of elatol, a chamigrene subclass of sesquiterpenes, required enantioselective decarboxylative allylation of a vinylogous ester derivative, an unexplored substrate class. The reaction proceeded with an 82% yield and 87%*ee* by using a more reactive phox ligand containing electron-withdrawing substituents. A previously unknown ring-closing metathesis to form a tetrasubstituted chlorinated olefin furnished the bicyclic core of elatol. The first total synthesis of enantioenriched (+)-elatol was achieved in an 11% yield over nine steps. The power of this methodology was illustrated in the synthesis of the marine diterpenoid (–)-cyanthiwigin F, a strategy which relied upon a double enantioselective desymmetrization. The pivotal palladium-catalyzed double allylation installs both stereogenic centres in a single step with excellent enantiocontrol (Scheme 3).

Metal-mediated catalysis proved to be a prevailing subject throughout the meeting, with its application being beautifully illustrated in the *Institute of Chemistry and Biochemistry Lecture* (IOCB) given by *Tamio Hayashi* (Kyoto University, Japan; Figure 3), ubiquitous in the field of asymmetric catalysis. He presented his conceptually new chiral diene ligands designed to provide high activity and selectivity to given reactions. These ligands were based on bicyclo[2.2.1]hepta-2,5-diene (nbd*), bicyclo[2.2.2]octa-2,5-diene (bod*)



Scheme 3.

or bicyclo[3.3.1]nona-2,6-diene (bnd*) skeletons and were shown to perform well in the rhodium-catalyzed asymmetric 1,4-addition of organoboron reagents to α,β-unsaturated ketones. In addition, high chemoselectivity and good yields were obtained with the equivalent silane reagents. More recently, these diene ligands were applied to the intramolecular asymmetric [4+2] cycloaddition of alkyne-1,3-dienes, again in high yield and enantioselectivity (90% yield, 96%*ee*; Scheme 4). This is a vast improvement when compared to the best-reported chiral phosphane ligand [(*R*,*R*)-MeDuPhos], which affords only a 9% yield and 44%*ee*. Finally, he exhibited some further structural developments in these remarkable ligands.

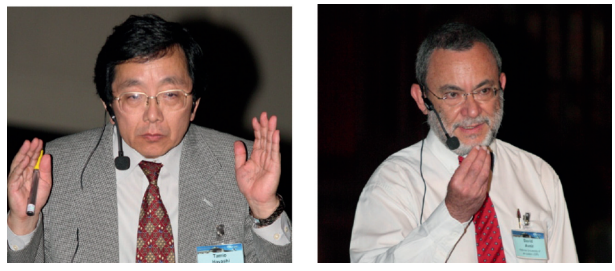
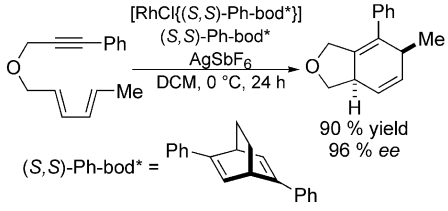


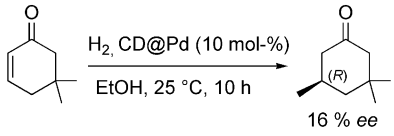
Figure 3. Tamio Hayashi (left) and David Avnir (right) trying to make their points.



Scheme 4.

David Avnir (Hebrew University of Jerusalem, Israel; Figure 3) delivered a fascinating lecture merging organic chemistry know-how with functional materials. His work focuses on combining the virtues of metals with the many and diverse properties of organic molecules to obtain novel catalysts. Firstly, the subject of encapsulation of an organic dopant within a metal was addressed. For example, doping

of silver with the dye congo red (CR@Ag) improved the performance of Ag as a catalyst for methanol oxidation when compared to Ag metal and CR-coated Ag. Secondly, the possibility of "acidic" Ag was presented by doping the metal with the polyacid Nafion (Nafion@Ag), which could be used as a heterogeneous acid catalyst. In addition, work using the metal as a matrix for heterogenizing homogeneous organometallic catalysts was presented. For example, [RhCl(cod){$Ph_2P(C_6H_4SO_3Na)$}] was entrapped within Ag ([Rh]@Ag) and utilized in the hydrogenation of styrene. It was found that the encapsulated catalyst gave the greatest conversion percentage compared to both the pure and surface-absorbed catalysts after the first cycle, and that the encapsulated catalyst was able to endure a further two cycles. The power of this methodology was elegantly demonstrated through encapsulation of chiral cinchona alkaloids within palladium. These hybrids were found to perform enantioselective catalytic hydrogenation (Scheme 5). Fascinatingly, the dopant could be removed to leave "chirally imprinted" palladium, shown by photoelectron emission spectroscopy, opening the doors to an entirely new type of asymmetric catalysis. The presentation culminated in a brief look into enzyme entrapment, where metals are able to provide a rigid cage through protein–metal interactions. These materials could one day find their way into bioactive implants and enzymatic electrodes.



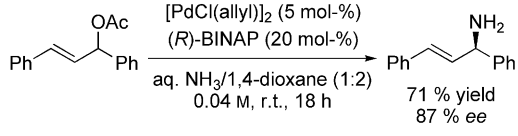
Scheme 5.

Juan Carretero (Autonomous University of Madrid, Spain) described his most recent work in applying new methodology to well-known reactions by developing the idea of the use of an auxiliary group. Here the use of a coordinating sulfonyl moiety enables both enantiocontrol and enhanced reactivity. The alkylation of aryl *N*-(2-pyridylsulfonyl)aldimines with organozinc bromides was shown to proceed in high yield with good functional-group compatibility and subsequent ease of deprotection. The reactivity of these aldimines (and ketimines) was accredited to their bidentate *N*,*N*-interaction with the copper catalyst as ascertained by X-ray crystallography and as exemplified by the lack of reaction with tolyl or thiophenylsulfonyl groups. The technique was also applied to the asymmetric aza-Diels–Alder reaction, with formation of highly functionalized piperidines in high yields and enantioselectivities by utilizing an (8-quinolyl)sulfonyl moiety.

The synthesis and functionalization of heterocyclic rings by classical methods is well established. *Sandro Cacchi* (University of Rome, Italy; Figure 4), however, presented his work on transition-metal catalysis as a useful tool in the construction of heterocycles. He commenced with palladium-catalyzed indole formation from ethyl-3-(*o*-trifluoroacetamidophenyl)-1-propargyl carbamate under mild conditions, which proceeded in good to excellent yield. More recently, his attention has turned from palladium to its more economically attractive neighbour copper, and the synthesis of polysubstituted pyrroles and pyridines, depending on the reaction conditions, by C–H activation. High yields of these useful synthetic intermediates from *N*-propargylic β-enaminones may be realized, and the reaction has a wide functional-group tolerance.

Figure 4. Animated discussions during the presentations of Sandro Cacchi (left) and Shu Kobayashi (right).

Shu Kobayashi (University of Kyoto, Japan; Figure 4) gave an excellent overview of his pioneering work undertaking organic reactions in water. The use of water as a solvent is clearly attractive for both economic, environmental and safety reasons, but also simplifies operations and purifications. Interestingly however, running reactions in water imparts a unique selectivity and reactivity upon the chemistry, unseen when using organic solvents. This was exemplified in previously unknown metal-catalyzed allylic amination reactions, in which aqueous ammonia was used for the synthesis of primary allylamines. It is noteworthy that the reaction did not proceed when ammonia gas was used and that the presence of water is essential for the reaction to occur. The first catalytic asymmetric variant was developed by using BINAP, giving an enantiomeric excess of 87% (Scheme 6). The addition of the metal hydroxides of allylboronates to aldehydes, known to proceed with high α-selectivity, can become highly γ-selective with the addition of water to the reaction mixture. Such carbon–carbon bond-forming reactions are often difficult to perform in aqueous media, even enzymatically. Kobayashi showed a new entry into water compatible Lewis acid catalysis in his work on unprecedented asymmetric Mukaiyama-type hydroxymethylation reactions in aqueous media. Despite their vast differences, both $Sc(OTf)_3$ and $Bi(OTf)_3$ gave excellent results in the presence of a chiral ligand, the latter actually being unstable in water alone. The methodology was expanded into the development of a novel Lewis acid surfactant combined catalysis (LACS), whereby small colloidal particles are formed, creating a hydrophobic pocket in



Scheme 6.

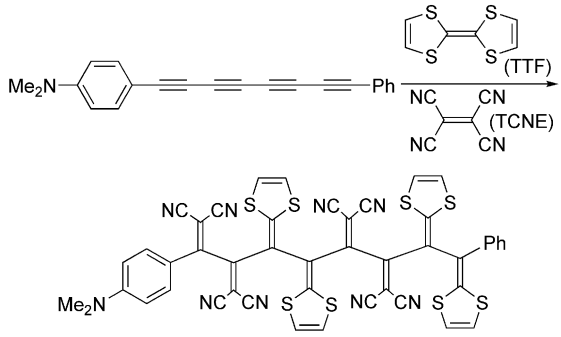
which catalysis occurs. Water also plays a key role in the asymmetric In^0-catalyzed α-addition of allylboranes to ketones, which proceeds with high *syn* selectivity.

Helma Wennemers (University of Basel, Switzerland; Figure 5), who was invited as part of a select group of *Young Talented Organic Chemists*, described the use of peptides in asymmetric catalysis. The easily tuneable bioinspired peptidic catalysts showed excellent diastereo- and enantioselectivity in both aldol reactions and 1,4-conjugate addition reactions of aldehydes to nitroolefins. A catalyst loading of just 1 mol-% gave comparable results to the 30 mol-% required for the equivalent proline-catalyzed reaction. Kinetic studies showed that the use of an excess amount of the nitroolefin rather than the aldehyde led to faster activity, reducing catalyst loading to just 0.1 mol-%. The substrate scope is broad; for example, nitroethylene can be used, with the resulting monosubstituted nitroaldehydes offering a convenient entry into γ^2-amino acids. In the second part of her talk, the use of peptides for the formation of Ag nanoparticles was described. The use of structurally diverse split-and-mix libraries identified which peptides were able to induce the formation of the Ag nanoparticles.

Figure 5. *Young Talented Organic Chemists* Helma Wennemers (left) and Magnus Rueping (right).

Magnus Rueping (RWTH Aachen University, Germany; Figure 5), another *Young Talented Organic Chemist*, began by presenting his novel enantioselective reduction of ketimines by using Hantzch dihydropyridine and a chiral Brønsted acid catalyst as an alternative to metal catalysis. He then enlightened us with his work into dual catalysis for the alkynylation of α-imino esters, where enantioselective activation is provided by the Brønsted acid, combined with metal-catalyzed alkynylation. It was proposed that the mechanism involved formation of a chiral metal (in this case silver) BINOL phosphate complex. In addition, he demonstrated the first enantioselective Brønsted acid catalyzed aza-Cope rearrangement with a range of readily accessible aromatic aldehydes.

The chemistry of push–pull organic chromophores and their importance towards optoelectronic systems was highlighted wonderfully by *François Diederich* (ETH Zürich, Switzerland; Figure 6). He demonstrated the highly efficient "click"-chemistry-like syntheses of nonplanar conjugated systems and allenoacetylenes. Nonplanar push–pull chromophores were elegantly synthesized by a [2+2] cycloaddition of electron-deficient alkenes with alkynes containing an electron-donating group. The intermediate cyclobutenes then undergo a retro-electrocyclization to form the desired nonplanar tetracyanobutadiene (TBCD) conjugated systems, with torsion angles of up to 45°. These compounds can be deposited as thin films with third-order optical nonlinearity by molecular beam epitaxy and have been investigated as waveguides for optical processing. This chemistry was further applied in an electronically controlled cascade reaction of a polyyne with an electron donor (TTF) and an electron acceptor (TCNE) to form conjugated donor–acceptor-substituted oligomers (Scheme 7). The introduction of allene moieties into TBCDs, and thus induction of chirality into the charge-transfer chromophore, was discussed, including extensive analysis by circular dichroism spectroscopy. Only one conformer was found to be present in solution, matching predictions made by DFT analysis.



Scheme 7.

Continuing along the theme of the development of π-conjugated systems, *Peter Bäuerle* (University of Ulm, Germany; Figure 6) provided insight into his work concerning oligothiophene-based organic solar cells. After summarizing advances made in the development of thiophene polymers and oligomers and dye-sensitized solar cells (DSSCs; coordinating ruthenium), he led us into his most recent work regarding functionalized dendritic oligothiophenes (DOTs). These DOTs are the third generation of advanced π-conjugated oligomers with a defined 3D nanoparticle structure. In this instance, trimethylsilyl-protected, branched terthiophene units were utilized as dendritic building blocks that advantageously facilitate further functionalization at the DOT periphery with dyes, redox and bioactive groups. These 3D semiconductors give intense, broad bands in their absorption spectra and are redshifted with increasing generational size. They also have optical band gaps comparable to that

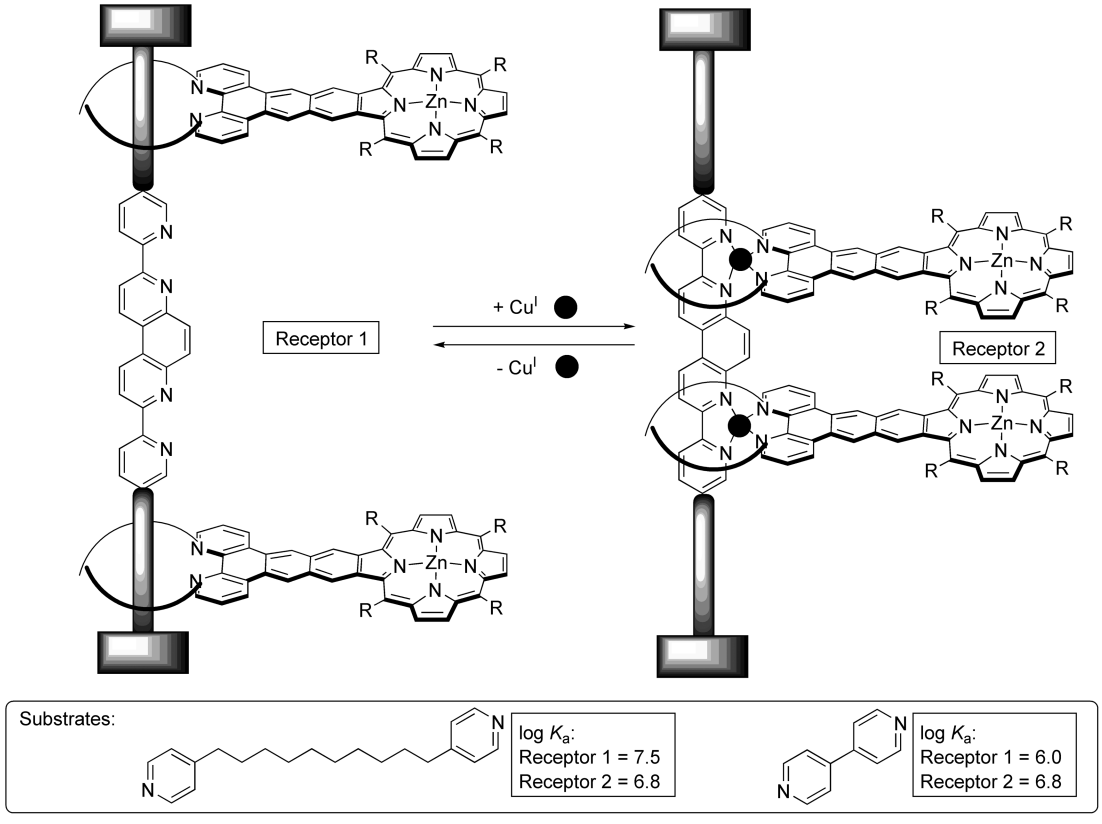
Figure 6. François Diederich (left) and Peter Bäuerle (right) involved in scintillating dialogue.

of linear semiconducting oligo- and polythiophenes, and once functionalized can reach an efficiency of 8.3% (in DSSCs).

The chemistry of topologically nontrivial molecules such as rotaxanes and catenanes is of much interest, both as a complex synthetic challenge and towards applications in molecular machinery. The history of the syntheses of these intriguing molecules and more recent, cutting-edge research into molecular machine prototypes were the subjects of the stimulating *New Journal of Chemistry Lecture* given by *Jean-Pierre Sauvage* (Le Bel Institute Strasbourg, France; Figure 7). Methods for synthesizing [2]-catenanes were described, such as "entwining and gathering" and "threading" around a CuI template, followed by removal of the copper ions by treatment with KCN. Various strategies for templating and closing catenane rings were discussed, including π–π stacking, H-bonding, Pd–N bonding and ring-closing metathesis. Other molecular topological achievements were also mentioned, including Sauvage's Trefoil knot and Stoddart's Borromean ring syntheses. Molecular machines were the next topic covered, which were defined as "multicomponent systems undergoing large amplitude motion under action of an external signal." Examples of such systems are abundant in nature; for instance, ATP synthase is a large multiprotein complex that acts as a rotary motor. Synthetic examples of molecular machines included [2]-catenanes, which rotate under electrochemical stimuli, and more recently, high-density (1011 bits cm^{-2}) electronic nanowire crossbar memories based on rotaxanes. New molecular machines based on 2D interlocking and threaded arrays were described, followed by the synthesis of a [3]-rotaxane, which was used as a "molecular press" (Scheme 8). This acts as an adjustable receptor for bispyridyl substrates with differing linker chain lengths. The selectivity of the receptor could be tuned by the addition and removal of CuI ions from the rotaxane.

Figure 7. Jean-Pierre Sauvage at a press conference explaining to journalists what a catenane is in the simplest and fastest way.

Janusz Jurczak (Institute of Organic Chemistry Warsaw, Poland) discussed some of the structural aspects of organic chemistry, specifically his work on electronically neutral anion receptors. Macrocycles generally dominate this field, but his recent work has centred on tailored, synthetically more accessible, simple, open-chain receptors. The focus is currently on pyrroles, pyridine, azulene and indole building blocks and examination of their anion affinity. The conformational preference, determined by molecular modelling of the receptor, was found to play an important role. These anion receptors were found to bind anions (BzO^-, $H_2PO_4^-$,



Scheme 8.

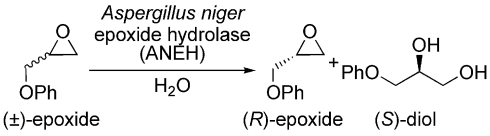
Cl^-) five times more strongly than their aniline analogues; however, the pyrrole ligand of the same type did not improve in a similar manner. It was previously observed that the adoption of a *syn–syn* conformation with convergent H-bonds was preferable for anion binding, but that the pyrrole ligand preferred an *anti–anti* orientation. He concluded by outlining his current work on 2,2′-diindolylmethane-based receptors that exhibit a high affinity for $H_2PO_4^-$, both in the presence of water and CD_3OH (binding studies are usually conducted in DMSO).

Barry Carpenter (Cardiff University, UK; Figure 8) strongly reaffirmed the need for science-based solutions for tackling global climate change. His talk centred on a potentially ingenious method for the removal of atmospheric CO_2 through photochemical reduction by amines. In the systems described, secondary and tertiary amines act as surrogates for H_2, which can reduce CO_2 to formic acid in the presence of a triaryl chromophore (OPP-3). Detailed mechanistic studies were described, in which the photochemical products and byproducts were identified by picosecond pulse IR spectroscopy. The results of these studies are being used to guide the synthesis of amines that give cleaner oxidation products, and hence, a more economically and ecologically viable process.

Figure 8. Barry Carpenter (left) and the *Lilly Distinguished Lectureship* awardee Manfred Reetz (right) during their presentations.

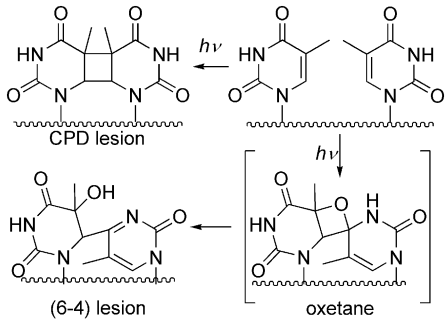
Georgios Vassilikogiannakis (University of Crete, Greece), the final *Young Talented Organic Chemist*, demonstrated the powerful synthetic utility of singlet oxygen for furnishing polyoxygenated motifs in natural products. Singlet oxygen (the first excited state of molecular oxygen) can react with a variety of unsaturated groups in organic molecules to yield peroxide products. This was demonstrated to great effect in the synthesis of the peroxyspiroketal-containing natural product premnalene A. The use of singlet oxygen in the syntheses of various furans was also discussed, along with elegant syntheses of the natural products pyrenolide D, crassalactone D, salinomycine, methofuran, pectenotoxin and scabrolide.

The *Lilly Distinguished Lectureship* was awarded to *Manfred Reetz* (Max Planck Institute for Coal Research, Germany; Figure 8), during which he presented his unconventional approach to asymmetric catalysis through directed evolution of enantioselective enzymes. Previous methods of harnessing Darwinian principles involved multiple rounds of error-prone PCR (epPCR), saturation mutagenesis and DNA shuffling, requiring numerous experiments and often identifying more mutations than necessary. As a result of these inefficient techniques, iterative saturation mutagenesis (ISM) was developed, encompassing CASTing (combinatorial active-site saturation test) for enantiocontrol and B-FIT for improved thermostability. For example, iterative CASTing was used repeatedly to further improve a mutant form of *Aspergillus niger* epoxide hydrolase (ANEH) until the desired improvement was realized. The wild type (WT) enzyme exhibits a selectivity factor, *E*, of 4.6 (*S*). Kinetic studies of the reaction in the presence of the mutated ANEH by using both the *R*- and *S*-epoxides independently revealed almost complete preference for the *S*-epoxide, with $E = 193$. Molecular dynamics calculations and X-ray analysis illustrated the position of the two substrates in the narrow binding pocket. It was observed that not only were the energetics of the reaction important, but that the proximity of the epoxide C atom to an attacking aspartate O atom was also important. Positioning of the disfavored *R*-enantiomer further from the reactive moiety by evolutionary processing made the reaction more difficult. He stressed that knowledge of the precise positioning of the reactant in the binding pocket is crucial for understanding the function of an enzyme (Scheme 9).



Scheme 9.

The study of DNA lesions and genome maintenance is vital in our understanding of DNA biochemistry and genetic diseases. *Thomas Carell* (LMU Munich, Germany; Figure 9) gave a fascinating account of his research into synthetic DNA lesion products and their biochemical activity. We learned that external and internal factors such as UV radiation, oxidation and anticancer chemotherapies (such as *cisplatin*) can cause upwards of 50000 DNA lesions per cell per day in humans. We are protected from this damage by two layers of defense − DNA repair enzymes (such as photolyases) and through lesion tolerance. Examples of UV-induced lesions are 6,4-photoproducts [(6–4) lesions] and cyclobutane pyrimidine dimers between adjacent thymine bases (CPD lesions), which can give rise to skin cancers (Scheme 10). Crystal structures were shown of a synthetic CPD lesion analogue bound to a DNA photolyase enzyme, and the mechanism for opening the CPD cyclobutane ring driven by blue-light irradiation was described. Results from another study into synthetic (6–4) lesions were presented, including a discussion of the cofactors involved in the repair process and the mechanism of repair through an oxetane intermediate catalyzed by histidine residues in the enzyme. Unlike DNA lesions, modifications to RNA are not generally lethal; for example, up to 20% of the bases in tRNA are modified in some way. Results from studies of labelled RNA lesion products were presented in the form of a "modome" analysis of the variable amounts of RNA lesions in different tissues.



Scheme 10.

Herman Overkleeft (Leiden University, The Netherlands) outlined his research into glucosylceramide (GC) metabolism, which is implicated in disorders such as Gaucher disease and type II diabetes. At least three enzymes, glucosylceramide synthase (GCS) and glucoceramidases GBA1 and GBA2, are believed to be involved in GC metabolism. Libraries of lipophilic iminosugars were synthesized and revealed to be selective inhibitors of the three target enzymes, showing therapeutic potential in the two aforementioned disease areas. The imino sugars are not only lead compounds in drug discovery, but they can also be considered as useful biological probes to further understand the enzymatic processes involved in GC metabolism.

Fredrik Almqvist (Umeå University, Sweden; Figure 9) described an alternative strategy for the development of antibacterial agents. Highly substituted ring-fused 2-pyridones, found to be active pilicides and curlicides, were designed to disarm rather than kill bacteria by targeting bacterial virulence, thereby reducing the occurrence of bacterial resistance. The heterocyclic scaffolds were synthesized by a novel enantioselective acyl–ketene imine cycloaddition reaction. This methodology allows facile structural variation to access libraries of compounds for biological evaluation. The pilicides were found to inhibit pili formation as well as adherence and biofilm formation in uropathogenic *E. coli* cells. This strategy allows for the study into the number of pili required for infection, which is not possible by using conventional knockout techniques.

Figure 9. Thomas Carell (left) and Fredrik Almqvist (right) trying to grab the attention of the audience.

Young chemists were well represented, with excellent contributions from graduate students *Yee Hwee Lim* working with *Professor K. C. Nicolaou* (Scripps Research Institute, USA) and *Professor V. Gouverneur* (University of Oxford, UK) and *Sara López-Tosco* working with *Dr. D. Tejedor* and *Dr. F. Garcia-Tellado* (Canary Islands Institute for Cancer Research, Spain). There were almost 600 poster presentations from over 50 countries, covering an extensive range of chemistry. Prizes sponsored by the *European Journal of Organic Chemistry*, Wiley-VCH, were presented by the journal Editor, *Haymo Ross* (Figure 10), and awarded to *L. Boissarie* (University of Geneva, Switzerland), *R. Correa da Costa* (University of Bristol, UK), *S. Kemme* (University of Freiburg, Germany) and *M. Kivala* (ETH Zurich, Switzerland). Prizes were also awarded by RSC Publishing and presented to *G. Owen-Smith* (University of Bristol, UK), *M. Schmid* (University of Regensburg, Germany), *L. Molnár* (CRC HAS, Hungary) and *P. Ostrovskis* (University of Riga, Latvia).

Figure 10. Haymo Ross, Editor of *EurJOC* (left), and *EurJOC* poster prize winners L. Boissarie (top middle), R. Correa da Costa (top right), S. Kemme (bottom middle) and M. Kivala (bottom right).

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