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Chemical Society Reviews

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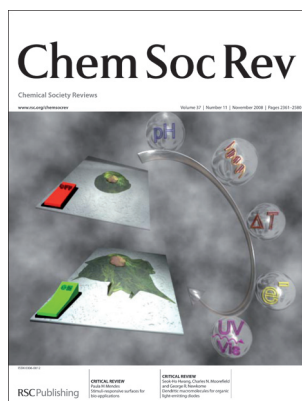
IN THIS ISSUE

ISSN 0306-0012 CODEN CSRVBR 37(11) 2361-2580 (2008)



Cover

The image shows the surface of a coupe, the trajectories of champagne droplets ejected from bursting bubbles, as seen through laser tomography techniques (G rard Liger-Belair, Fabien Beaumont, Guillaume Polidori). Image reproduced by permission of G rard Liger-Belair, Guillaume Polidori and Philippe Jeandet from *Chem. Soc. Rev.*, 2008, **37**, 2490.



Inside cover

See Paula M Mendes, page 2512. In recent years, stimuli-responsive surfaces have been used to modulate biological interactions, offering an unprecedented ability to control cell adhesion and migration on surfaces. Image reproduced by permission of Paula M Mendes from *Chem. Soc. Rev.*, 2008, **37**, 2512.

CHEMICAL SCIENCE

C81

Drawing together research highlights and news from all RSC publications, *Chemical Science* provides a 'snapshot' of the latest developments across the chemical sciences, showcasing newsworthy articles and significant scientific advances.

Chemical Science

November 2008/Volume 5/Issue 11

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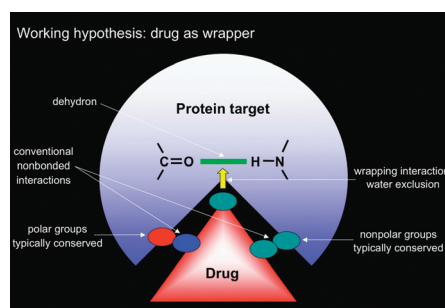
TUTORIAL REVIEWS

2373

Protein wrapping: a molecular marker for association, aggregation and drug design

Ariel Fern andez* and Alejandro Crespo

We survey the concept of protein wrapping, a descriptor of packing quality, and assert its relevance in the contexts of misfolding, aggregation and drug design.



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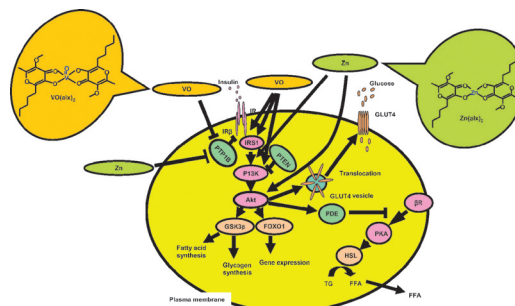
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2383

Current state for the development of metallopharmaceutics and anti-diabetic metal complexes

Hiromu Sakurai,* Yutaka Yoshikawa and Hiroyuki Yasui

The history of the development of metallopharmaceutics and the current state of development of metal complexes with anti-diabetic and anti-metabolic syndrome activities are reviewed.

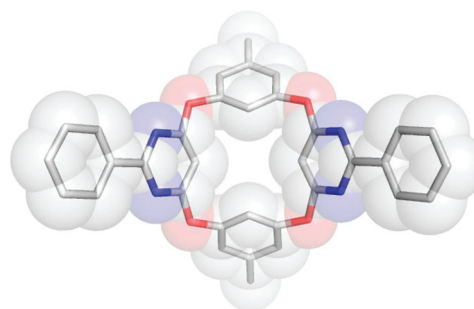


2393

Oxacalix[n](het)arenes

Wouter Maes and Wim Dehaen*

Recent advances in the synthesis and applications of oxacalix[n]arenes are described, expanding the scope of the field from a merely synthetic to a more applied branch of supramolecular chemistry.

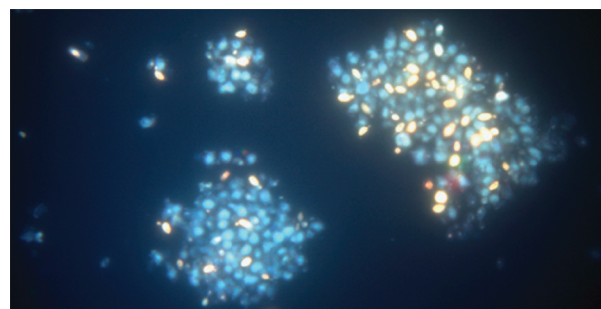


2403

Bio-directed synthesis and assembly of nanomaterials

Wendy J. Crookes-Goodson, Joseph M. Slocik and Rajesh R. Naik*

This tutorial review highlights how organisms synthesize nanomaterials *in vivo* as well as how the natural world has inspired researchers to pursue the *in vitro* synthesis of materials using biological molecules.

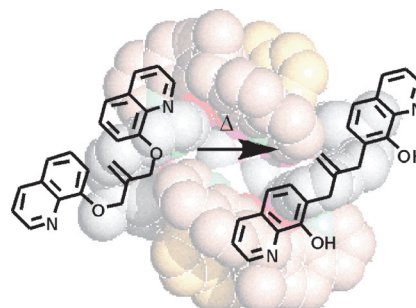


2413

The tandem Claisen rearrangement in the construction of building blocks for supramolecular chemistry

Kazuhisa Hiratani* and Markus Albrecht*

The tandem Claisen rearrangement in supramolecular chemistry.



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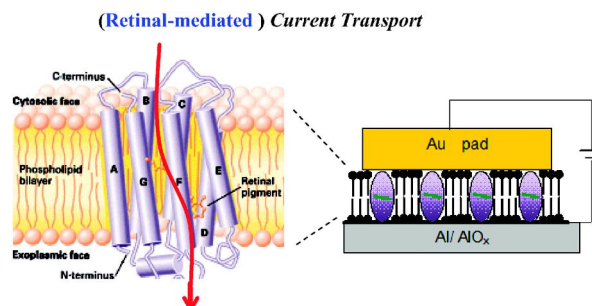
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2422

Bacteriorhodopsin as an electronic conduction medium for biomolecular electronics

Yongdong Jin,* Tal Honig, Izhar Ron, Noga Friedman, Mordechai Sheves* and David Cahen*

This tutorial review discusses bacteriorhodopsin as a medium for biomolecular optoelectronics, emphasizing ways in which it can be interfaced, especially as a thin film, solid-state current-carrying electronic element.

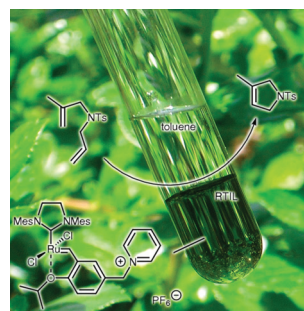


2433

Olefin metathesis in ionic liquids

Paweł Śledź,* Marc Mauduit* and Karol Grela*

This review covers the use of ionic liquids (IL) as (co)solvents for the olefin metathesis reaction. It is expected that the application of IL as well as the development of IL-enabled catalysts and separation techniques will create a green aspect to this important methodology.



2443

Applications of biocatalysis in fragrance chemistry: the enantiomers of α -, β -, and γ -irones

Elisabetta Brenna,* Claudio Fuganti and Stefano Serra

Biocatalysis can help Nature in the production of chiral odorous molecules: the case of irones.

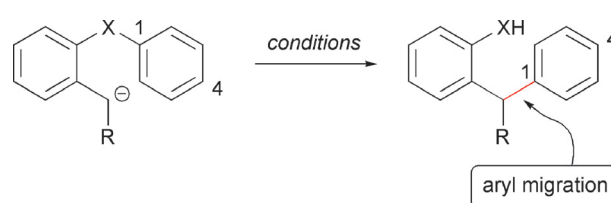


2452

A truce on the Smiles rearrangement: revisiting an old reaction—the Truce–Smiles rearrangement

Timothy J. Snape*

The Truce–Smiles rearrangement is reviewed, demonstrating its potential in the development of new synthetic methods.



The Truce–Smiles rearrangement

Dynamic Stereochemistry of Chiral Compounds

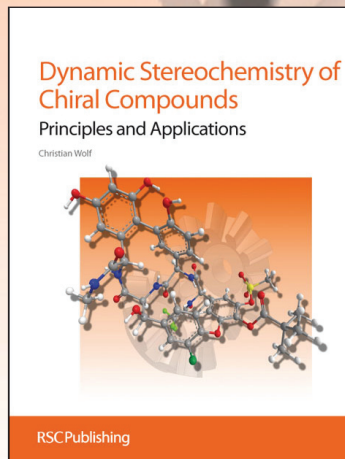
This book provides an overview of fundamental concepts of asymmetric synthesis highlighting the significance of stereochemical and stereodynamic reaction control. Topics include kinetic resolution (KR), dynamic kinetic resolution (DKR), dynamic kinetic asymmetric transformation (DYKAT), and dynamic thermodynamic resolution (DTR). In-depth discussions of asymmetric synthesis with chiral organolithium compounds, atropisomeric biaryl synthesis, self-regeneration of stereogenicity (SRS), chiral amplification with chiral relays and other commonly used strategies are also provided. Particular emphasis is given to selective introduction, interconversion and translocation of central, axial, planar, and helical chirality.

A systematic coverage of stereochemical principles and stereodynamic properties of chiral compounds guides the reader through the book and establishes a conceptual linkage to asymmetric synthesis, interconversion of stereoisomers, molecular devices that resemble the structure and stereomutations of propellers, bevel gears, switches and motors, and topologically chiral assemblies such as catenanes and rotaxanes. Racemization and diastereomerization reactions of numerous chiral compounds are discussed as well as the principles, scope and compatibility of commonly used analytical techniques.

- More than 550 figures, schemes and tables illustrating mechanisms of numerous asymmetric reactions and stereomutations of chiral compounds
- Technical drawings illustrating the conceptual linkage between macroscopic devices such as turnstiles, ratchets, brakes, bevel gears, propellers or knots and molecular analogs
- More than 3000 references to encourage further reading and facilitate additional literature research
- A comprehensive glossary with stereochemical definitions and terms which facilitate understanding and reinforce learning

This book will be of particular interest to advanced undergraduates, graduates and professionals working and researching in the fields of synthetic organic chemistry and stereochemistry.

030804



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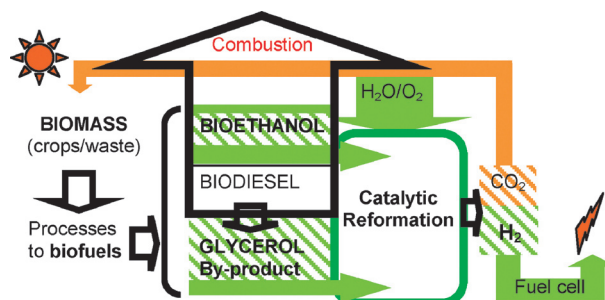
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2459

Use of biofuels to produce hydrogen (reformation processes)

Pilar Ramírez de la Piscina* and Narcís Homs*

Open routes to hydrogen production from biofuels for clean and renewable-based energy.



2468

Determination of mycotoxins in human foods

Gordon Seymour Shephard*

Analysis of naturally occurring fungal toxins, which impact negatively on human and animal health, is an essential component of food safety.



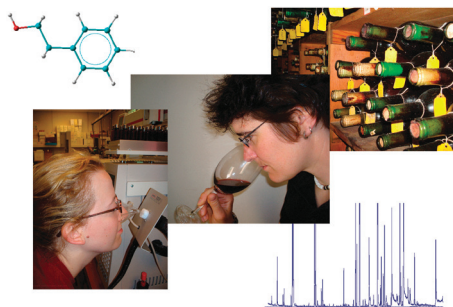
CRITICAL REVIEWS

2478

Wine flavor: chemistry in a glass

Pavla Polášková, Julian Herszage and Susan E. Ebeler*

This critical review provides information on multidisciplinary approaches for understanding the complex chemistry of wine flavor.

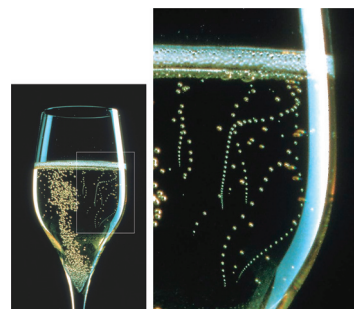


2490

Recent advances in the science of champagne bubbles

Gérard Liger-Belair,* Guillaume Polidori and Philippe Jeandet

This critical review summarizes recent advances obtained during the past decade concerning the physicochemical processes behind the nucleation, rise, and burst of bubbles found in glasses poured with champagne and sparkling wines. Graphic © Alain Cornu/Collection CIVC.





Chemistry-Biology Interface

Chemistry-Biology Interface theme issue

This theme issue covers topical areas at the chemistry–biology interface from a chemical perspective. The biological consequences of specific molecular interactions have long been a part of scientific (and non-scientific) activities throughout human history. The last century witnessed a myriad of discoveries in the life sciences at molecular detail, and the associated growth of the pharmaceutical and biotech industries. This century has seen a further growth in the field with a resultant increase in publications and journals.

Reviews include:

Nucleic acid encoding to program self-assembly in chemical biology

Zbigniew L. Pianowski and Nicolas Winssinger

Chemical technologies for probing embryonic development

Ilya A. Shestopalov and James K. Chen

Interspecies and interkingdom communication mediated by bacterial quorum sensing

Colin A. Lowery, Tobin J. Dickerson and Kim D. Janda

Small molecule inhibition of microbial natural product biosynthesis—an emerging antibiotic strategy

Justin S. Cisar and Derek S. Tan

Identification of the cellular targets of bioactive small organic molecules using affinity reagents

Benjamin J. Leslie and Paul J. Hergenrother

Expanding dialogues: from natural autoinducers to non-natural analogues that modulate quorum sensing in Gram-negative bacteria

Grant D. Geske, Jennifer C. O'Neill and Helen E. Blackwell

Guest editor:



David Spring
University of Cambridge, UK

"The interface with biology is a fertile scientific pursuit for chemists"

060833

See also:

Molecular BioSystems issue 6, 2008 – Emerging Investigators theme issue

For more details see www.molecularbiosystems.org/ei

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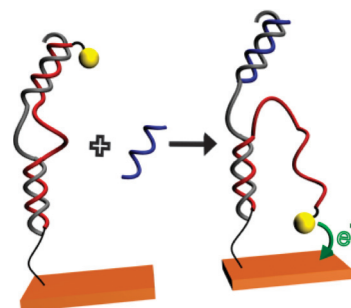
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2512

Stimuli-responsive surfaces for bio-applications

Paula M Mendes

This critical review focuses on the recent progress in the preparation of stimuli-responsive surfaces based on self-assembled monolayers or thin polymer films, and highlights their applications in biological environments.

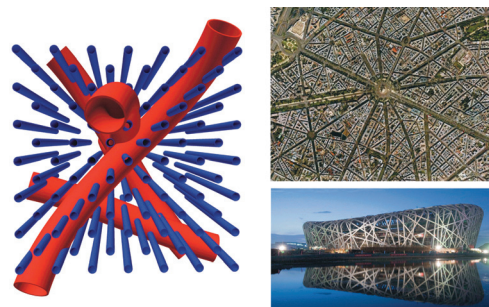


2530

Hierarchical zeolites: enhanced utilisation of microporous crystals in catalysis by advances in materials design

Javier Pérez-Ramírez,* Claus H. Christensen, Kresten Egeblad, Christina H. Christensen and Johan C. Groen

This critical review examines recent advances in the rapidly evolving area of zeolites with improved accessibility and molecular transport, establishing a link between available synthesis strategies, materials properties, and catalytic function.

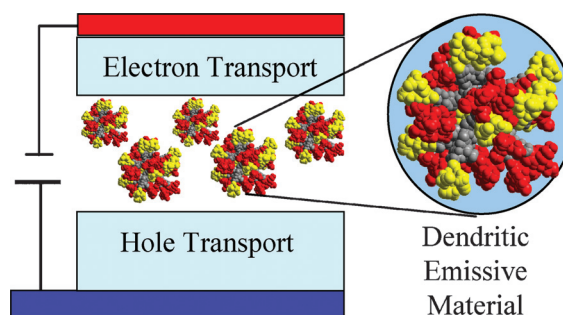


2543

Dendritic macromolecules for organic light-emitting diodes

Seok-Ho Hwang, Charles N. Moorefield and George R. Newkome*

Branched architectures 'shine brightly' in the quest for efficient and effective components in organic light-emitting diodes.

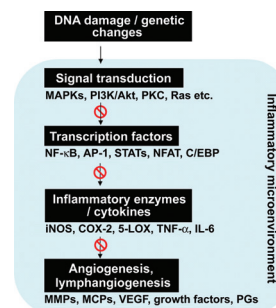


2558

Chemopreventive effects of natural dietary compounds on cancer development


Min-Hsiung Pan and Chi-Tang Ho*

Chemoprevention, a relatively new and promising strategy to prevent cancer, is defined as the use of natural dietary compounds and/or synthetic substances to block, inhibit, reverse, or retard the process of carcinogenesis. The three critical steps in this process for several types of human cancer formation are initiation, promotion and progression, and invasion and metastasis.



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Fitzsimmons Los Alamos National Laboratory tel. 505-665-4045 fitz@lanl.gov</p> <p>Young-Chang Joo Seoul National University tel. 82-2-880-8986 ycjoo@snu.ac.kr</p> <p style="text-align: center;">***</p> <p>For Additional Information, visit the MRS Web site at www.mrs.org/meetings/ or contact:</p> <p>Member Services Materials Research Society 506 Keystone Drive Warrendale, PA 15086-7573 Tel 724-779-3003 Fax 724-779-8313 info@mrs.org</p>	<p>ELECTRONICS, PHOTONICS, AND MAGNETISM</p> <p>A: Performance and Reliability of Semiconductor Devices</p> <p>B: Transparent Conductors and Semiconductors for Optoelectronics</p> <p>C: Theory and Applications of Ferroelectric and Multiferroic Materials</p> <p>D: Rare-Earth Doping of Advanced Materials for Photonic Applications</p> <p>E: Materials and Technologies for 3-D Integration</p> <p>F: Low-Cost Solution-Based Deposition of Inorganic Films for Electronic/Photonic Devices</p> <p>G: Organic and Hybrid Materials for Large-Area Functional Systems</p> <p>H: Physics and Technology of Organic Semiconductor Devices</p> <p>I: Reliability and Properties of Electronic Devices on Flexible Substrates</p> <p>J: Material Science for Quantum Information Processing Technologies</p> <p>K: Magnetic Nanostructures by Design</p> <p>L: New Materials with High Spin Polarization and Their Applications</p> <p>ENERGY AND THE ENVIRONMENT</p> <p>M: Energy Harvesting—Molecules and Materials</p> <p>N: Next-Generation and Nano-Architected Photovoltaics</p> <p>O: Structure/Property Relationships in Fluorite-Derivative Compounds</p> <p>P: Photovoltaic Materials and Manufacturing Issues</p> <p>Q: Scientific Basis for Nuclear Waste Management XXXII</p> <p>R: Materials for Future Fusion and Fission Technologies</p> <p>S: Solid-State Ionics</p> <p>T: Mobile Energy</p> <p>U: Advanced Intermetallic-Based Alloys for Extreme Environment and Energy Applications</p>	<p>ENGINEERED MATERIALS AND MODELING</p> <p>V: Materials, Devices, and Characterization for Smart Systems</p> <p>W: Computational Materials Design via Multiscale Modeling</p> <p>Y: Biomineral Interfaces—From Experiment to Theory</p> <p>Z: Mechanics of Biological and Biomedical Materials</p> <p>AA: Materials for Optical Sensors in Biomedical Applications</p> <p>BB: Polymer-Based Smart Materials—Process, Properties, and Application</p> <p>CC: Design, Fabrication, and Self Assembly of “Patchy” and Anisometric Particles</p> <p>DD: Materials in Tissue Engineering</p> <p>NANOSCIENCE</p> <p>EE: Nano- and Microscale Materials—Mechanical Properties and Behavior under Extreme Environments</p> <p>FF: Nanofunctional Materials, Structures, and Devices for Biomedical Applications</p> <p>GG: Microelectromechanical Systems—Materials and Devices II</p> <p>HH: Advances in Material Design for Regenerative Medicine, Drug Delivery, and Targeting/Imaging</p> <p>II: Bio-inspired Transduction, Fundamentals, and Applications</p> <p>JJ: Nanotubes, Nanowires, Nanobelts, and Nanocoils—Promise, Expectations, and Status</p> <p>KK: Transport Properties in Polymer Nanocomposites</p> <p>LL: Nanowires—Synthesis, Properties, Assembly, and Application</p> <p>MM: Applications of Group IV Semiconductor Nanostructures</p> <p>NN: In-situ Studies across Spatial and Temporal Scales for Nanoscience and Technology</p> <p>OO: Grazing-Incidence Small-Angle X-Ray Scattering</p> <p>PP: Solid-State Chemistry of Inorganic Materials VII</p> <p>QQ: Synthesis and Processing of Organic and Polymeric Functional Materials for a Sustainable Energy Economy</p> <p>RR: Artificially Induced Grain Alignment in Thin Films</p> <p>SS: Selecting and Qualifying New Materials for Use in Regulated Industries</p> <p>TT: Local Structure and Dynamics in Amorphous Systems</p> <p>GENERAL INTEREST</p> <p>X: Frontiers of Materials Research</p>	<p>Symposium/Tutorial Program</p> <p>Available only to meeting attendees, the symposium tutorials will concentrate on new, rapidly breaking areas of research.</p> <p>Exhibit</p> <p>A major exhibit encompassing the full spectrum of equipment, instrumentation, products, software, publications, and services is scheduled for December 2-4 in the Hynes Convention Center. Convenient to the technical session rooms and scheduled to complement the program, the MRS Fall Exhibit offers everything you need all under one roof.</p> <p>Publications Desk</p> <p>A full display of over 950 books will be available at the MRS Publications Desk. Symposium Proceedings from the 2007 MRS Fall Meeting and 2008 MRS Spring Meeting will be featured.</p> <p>Student Opportunities</p> <p>Graduate students planning to attend the 2008 MRS Fall Meeting are encouraged to apply for a Symposium Assistant position and/or a Graduate Student Award. Applications will be accessible on the MRS Web site by June 1.</p> <p>Career Center</p> <p>A Career Center for MRS members and meeting attendees will be open Tuesday through Thursday.</p>

Chemical Science

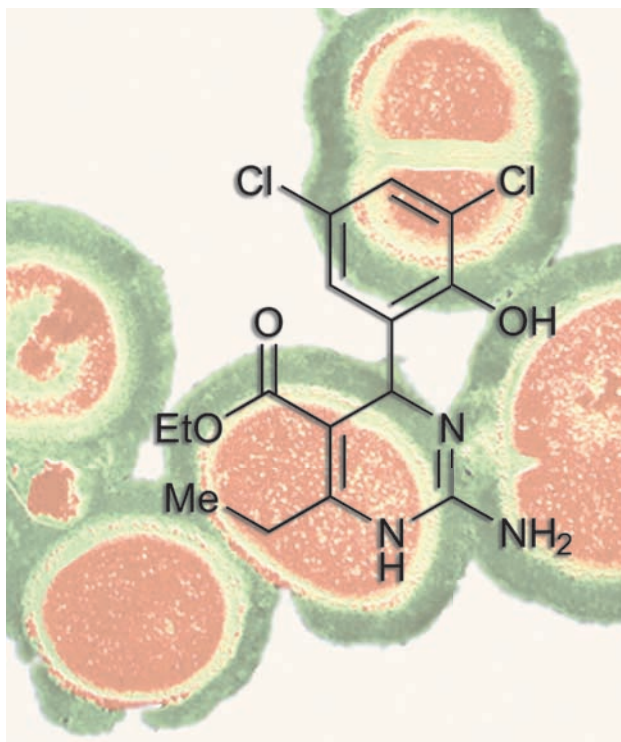
MRSA-beating compounds are key targets in human medicine

Inhibiting the spread of superbugs

UK chemists have found a small molecule with the potential to overcome one of the most serious problems facing the healthcare profession today – the spread of the deadly infection MRSA.

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a multidrug resistant strain of the common *S. aureus* bacterium that causes difficult-to-treat infections in humans. The development of new antibacterial agents to overcome this and other ‘superbugs’ are key targets in human medicine. With this in mind David Spring and colleagues at the University of Cambridge, UK, have used diversity-orientated synthesis to identify a small molecule which can inhibit the enzyme that controls cell division in an epidemic strain of MRSA.

The diversity-oriented synthesis used by Spring involved making a library of 200 structurally-diverse compounds and screening them for the required antibacterial activity against two epidemic strains of MRSA. The successful compounds



Emmacin (above) was the most potent anti-MRSA agent found

were narrowed down to those with key frameworks and functional groups and were then subjected to further screening. The most potent of these was a substituted dihydropyrimidine named emmacin.

In further tests Spring showed that emmacin can selectively inhibit the key dihydrofolate reductase (DHFR) enzyme in an epidemic strain of MRSA, known as EMRSA-16. He also found that it exhibits no cytotoxic properties in mammalian systems.

Spring suggests that emmacin may be representative of a whole new class of bacteria selective DHFR inhibitors which could be exploited in the development of critically needed new antibacterial agents. ‘Bacteria are becoming resistant to DHFR inhibitors, so the more classes of compound which we can discover, the better we can tackle this problem,’ he adds.

Richard Kelly

Reference

E E Wyatt *et al.*, *Chem. Commun.*, 2008, 4962 (DOI:10.1039/b812901k)

In this issue

Cancer cells need salting before cooking

Nanoparticle thermotherapy has ‘great potential’ for biomedical research

Copper-free clicking

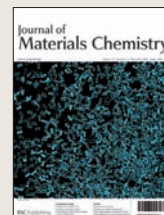
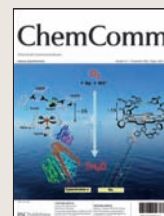
Non-toxic click chemistry reactions are being explored

Instant insight: Is your food safe to eat?

Gordon Shephard highlights the analytical methods used to ensure our food is free from the natural toxins made by fungi

Interview: Chemistry is the business

A V Rama Rao talks to Joanne Thomson about how science has shaped development in India



A snapshot of the latest developments from across the chemical sciences

Research highlights

New computer software speeds up the analysis of X-ray diffraction patterns

Crystal phases get ID'd

It is now easier to automatically ID crystal phases in zeolites, thanks to scientists in Spain

Laurent Baumes at the University of Valencia and co-workers have developed a new method for automatically deciphering X-ray diffraction patterns – allowing crystallographic phases to be identified quickly and reliably.

X-ray diffraction is used for a wide range of purposes, from routine characterisation in industrial production control through to in-depth research investigations of the most complex high-technology materials. However, the analysis of the diffraction data can be very complex explains Baumes. The synthesis of crystalline materials such as zeolites often produces a mixture of phases, he says, which need to be identified in order to determine how different synthetic methods influence the structure



obtained and also to identify new phases that may have been made.

Baumes' method, called adaptable time warping, is a piece of advanced computer software that can be coupled with existing high throughput synthesis

Zeolite structures can now be rapidly identified

Reference
L A Baumes *et al.*,
CrystEngComm, 2008, **10**, 1321
(DOI: 10.1039/b812395k)

technologies to help speed up the whole process of experimental and data analysis.

The new technique has been compared with existing software, says Baumes, and it shows a clear improvement in the error rate which is even more apparent when there is a mixture of crystalline and noncrystalline phases.

'The main application is the reduction of the time to market for new materials through the use of advanced software combined with high throughput technologies,' says Baumes.

Stephan Schunk, a scientist at hte - the high throughput experimentation company, Heidelberg, Germany, says 'the work is a breakthrough'. 'It enables the scientist to embark on complex synthetic programs and puts him in a position of ease and comfort when analysing the data,' he adds.
Sarah Dixon

Nanoparticle thermotherapy has 'great potential' for biomedical research

Cancer cells need salting before cooking

Korean scientists have used table salt to help them move closer to creating a porous silicon nanobomb that will literally blow up cancerous cells.

Thermotherapy – that uses near infrared (NIR) light to destroy cells – stopped being used in the 1990s, but thanks to new research is making a comeback as a possible alternative to currently available therapies for removing cancerous cells. Recently agents such as carbon nanotubes – that emit heat after irradiation with NIR – have been tried in combination with thermotherapy to kill cancer cells selectively.

Last year Chongmu Lee and co-workers at Inha University, Incheon, found that porous silicon offered a non-toxic and biodegradable alternative to carbon nanotubes for killing breast cancer cells. Now in vitro tests have shown that a suspension of porous



silicon in sodium chloride solution offers better results still, say the researchers.

The researchers avoid killing healthy cells by taking advantage of the folic acid- and antibody-receptors that are over abundant in most cancer cells. They pre-treat the porous silicon in sodium chloride solution with folic acid or

Salt improves the performance of porous silicon as a thermotherapy agent

Reference
C Lee *et al.*, *J. Mater. Chem.*,
2008, **18**, 4790 (DOI:10.1039/
b808500e)

antibodies, so that the agent binds selectively to the cancer cells before irradiation.

'Porous silicon can substantially lower the illumination intensities of NIR necessary to obtain a heating effect sufficient to destroy cancer cells down to a level which can be actually used in the clinic,' says Lee.

Lisa DeLouise, an expert in porous silicon at the University of Rochester Medical Centre in the US, says 'nanoparticle thermotherapy is an emerging field with great potential for biomedical research'.

Lee is continuing his research with in vivo tests, before moving on to clinical trials. He will go on to use the explosive properties of porous silicon to form a nanobomb for cancer treatment by finding a biocompatible oxidant to trigger heating. He is also working on a similar titanium dioxide system.
Sylvia Pegg

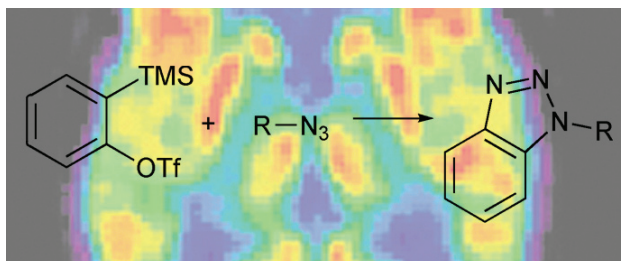
Non-toxic alternatives to current click chemistry are being explored

Copper-free clicking

Dutch scientists have developed a biologically-friendly click reaction which may lead to new tracers for improving the 3D imaging of cancerous tumours.

Click chemistry often includes copper catalysts that remove the need for the high temperatures and pressures. But copper is toxic to most living things so copper-free alternatives are highly sought after.

To achieve this Ben Feringa, University of Groningen, and his team reacted a benzene ring, substituted with two leaving groups, with various functionalised azides to make benzotriazoles. The reactions could be activated using fluoride salts in combination with a complementary crown ether to give the product in yields of up to 82 per cent. This was achieved in less than two hours without the need for a copper catalyst, or elevated temperatures and pressures.



Feringa warns that this is just a first step in the right direction for ‘developing alternatives to current click chemistry’. ‘The problem with the use of this method in the context of living organisms would be that, although it is fast and does not need copper, fluoride is still needed to generate the reactive benzyne and we do not know if it will work in the aqueous environment of a cell.’

David Jackson, Syngenta, Muenchwilen, Switzerland

Benzotriazoles can be made using a copper-free click reaction

Reference
L Campbell-Verduyn *et al*, *Org. Biomol. Chem.*, 2008, **6**, 3461 (DOI: 10.1039/b812403e)

– whose interests include reaction optimisation and clean chemistry – is impressed with the work: ‘The benzotriazole unit continues to be of significant interest as a component in new potential new products in the life sciences industry. The triazole unit is particularly tricky to build at a multi kilogram scale due to the instability of building blocks and reagents. All new mild methods leading to their formation are sure to find applications.’

‘With this method in hand our first goal is to introduce radiolabels like fluoride into relevant compounds for positron emission tomography (PET) tracer studies,’ says Feringa. ‘We are also exploring its use in labelling a range of bioactive compounds where copper-catalysed click reactions are currently used.’

Christina Hodkinson

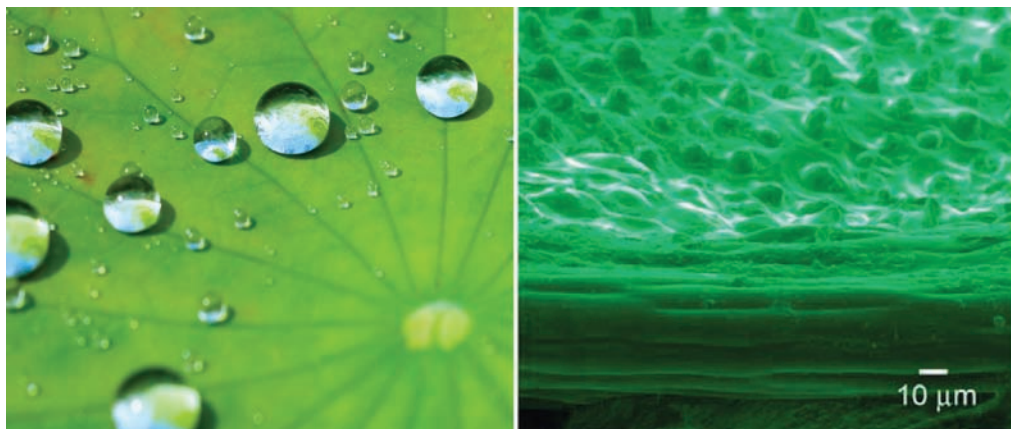
Lotus leaves are cleverly designed to prevent water flowing onto them

How water leaves lotus leaves

The mystery of how superhydrophobic lotus leaves remain completely dry whilst floating on water has been solved by Chinese scientists.

The top of a floating lotus leaf is a famous example of a superhydrophobic surface that sheds water, and has been used as a model for technologies such as self-cleaning windows. The leaf is covered in a rough surface of waxy projections, which causes water to form beads and slide off. Now Lei Jiang of the Chinese Academy of Sciences in Beijing and colleagues have found out why, when floating, no water flows onto the leaf.

Electron microscopy showed that, close to the leaf edge the projections are replaced by a smooth surface of folds and grooves, preventing the reverse-flow of water droplets. This means that the leaf is 50 per cent more resistant to submersion than a model leaf with a smooth surface.



Folds and grooves at the leaf margin help keep it dry

Jiang suggests that, just as the lotus leaf surface has provided inspiration for superhydrophobic surfaces, the leaf margin can serve as a model in applications such as tubes or microfluidic channels which require clean outflow or directional repellancy.

Abraham Marmur, a professor of water science and technology

at Technion–Israel Institute of Technology, Haifa, says that ‘the authors should be congratulated for opening a new angle for looking at the wonders of the lotus leaf’.

Michael Townsend

Reference
J Zhang *et al*, *Soft Matter*, 2008, **4**, 2232 (DOI: 10.1039/b807857b)

Lead contamination concerns at military training grounds lead to new detonators

Environmentally friendly explosives

Scientists in Germany have made lead-free detonators for reducing the environmental impact of military explosives.

Detonators contain primary explosives which can be easily ignited by a physical or electric stimulus. They are used to trigger the explosion of more stable energetic materials in guns and hand grenades. Currently, almost all primary explosives are based on lead azide which causes concern for human health and the environment.

Thomas Klapötke and colleagues at the Ludwig-Maximilian University of Munich made alkali metal salts as a replacement for lead azide. 'Lead is a toxic heavy metal and there are concerns about lead concentration at military training grounds,' says Klapötke. Over 90 000 hand grenades are used at these sites every year, explains Klapötke, therefore it is important to try to make the soldiers lives safer and healthier by removing toxic substances.



Klapötke's team made a family of alkali metal salts with the energetic 5-nitrotetrazolate anion. The salts with the harder lithium and sodium cations were found to contain crystal water, which gives them low sensitivity towards shock and friction. The rest of the alkali metal salts form as the anhydrous species, and show increased explosive sensitivities making them more

Alkali metal-based primary explosives are less toxic than the current lead-based ones

Reference
T M Klapötke, C M Sabaté and J M Welch, *Dalton Trans.*, 2008, DOI: 10.1039/b811410b

useful as prospective replacements for commonly used primary explosives.

Klapötke says that the new primary explosives are good enough for military use, however more work is needed to improve their thermal stability for use in harsh conditions such as for oil drilling. In the future we also hope to look into environmentally friendly replacements for other explosives such as perchlorates which are used as oxidisers in pyrotechnics and solid rocket boosters, he adds.

Joseph Backofen, BRIGS Co., Herndon, US, an expert in ballistics, comments 'this work represents a clear path towards developing new energetic materials that are free from constituents deemed harmful to their users during routine work. This issue is important in primers used in rifle and pistol ammunition used in indoor training ranges by police and military personnel.'

Sarah Dixon

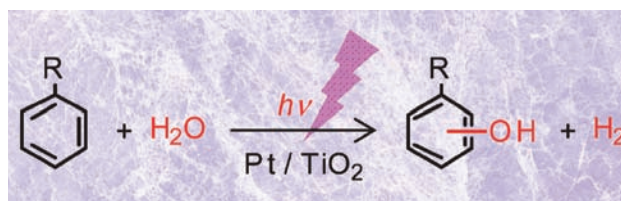
Tap water proves its worth in the synthesis of phenols

Water to wine...well alcohols actually

Japanese scientists have unleashed the power of water to improve the selectivity and green credentials of the synthetic route to industrially-important phenols.

Hisao Yoshida and colleagues from Nagoya University have developed a photocatalyst that activates water to oxidise functionalised aromatic rings in a selective manner.

Phenols are currently made using a multistep process which consumes a significant amount of energy. Selectivity is another well-known disadvantage of this route, as the side chains often oxidise in preference to the aromatic ring. Much research has been done into developing one-step, environmentally-friendly and more efficient routes which involve the direct oxidation of aromatic rings. However to date selectivity has remained an issue.



Now, Yoshida has overcome this using a platinum-loaded titanium oxide catalyst that is activated by illumination with the appropriate wavelength of light. The activated catalyst then converts water into an oxygen species that selectively reacts with an aromatic ring to make the required phenol, with hydrogen as the waste product.

Added bonuses of this route include mild reaction conditions – room temperature and atmospheric pressure – and removal of the need for expensive or hazardous oxidants. Additionally Yoshida found that the intensity and

A photocatalyst activates water to selectively oxidise aromatic rings

Reference
H Yoshida *et al.*, *Chem. Commun.*, 2008, 4634 (DOI: 10.1039/b811555a)

wavelength of the light can be varied to finely control the reaction products.

Yoshida recognises that the rate of the reaction needs to be improved before this can be a useful industrial process. However, he says that 'our findings provide an important principle which may be widely valuable for many kinds of undiscovered chemical syntheses, especially selective oxidation.'

Stephen Poulston, an expert in photocatalysis at Johnson Matthey, Reading, UK, agrees: 'It is encouraging to see potential applications for photocatalysis beyond the more well-established research.' 'I think the challenge with this reaction, which is common to most photocatalytic processes, is how to scale the reaction up and how to increase the reaction rate,' he adds.

May Copesey

Is your food safe to eat?

Gordon Shephard, South African Medical Research Council, Cape Town, highlights the analytical methods used to ensure our food is free from the natural toxins produced by fungi

Food is the essence of life, yet the majority of people give little thought to the role analytical chemistry plays in ensuring our food is safe to eat. When food safety issues are raised, it is normally the perceived problems of pesticide – or other man-made chemical – residues in our foods causing concern. Yet natural toxins, produced by a range of microbiological organisms, are actually more potent toxins and carcinogens and therefore a greater threat to food safety.

Amongst these natural toxins are the mycotoxins, secondary metabolites of filamentous fungi – more commonly known as mould. These can infect agricultural products both in the field, during plant growth, as well as in poorly stored produce. Many of the mycotoxins are extremely stable and can survive in the agricultural raw material through to the finished product on the supermarket shelf. Similarly, their presence in animal feed can result in the carry-over of the toxin or its metabolites into animal products for human consumption.

Although practically unknown in the developed world due to the vigilance of food safety authorities, human morbidity and mortality due to mycotoxin exposure is widespread in developing countries – especially in communities that are self-sufficient.

The mycotoxins have a diverse range of chemical structures and therefore biological effects. Although many hundreds of these toxins are known, researchers and food safety authorities concentrate on those produced by fungal pathogens of major crops – aflatoxins, fumonisins, trichothecenes (especially deoxynivalenol and T-2 toxin),



Maize kernels infected with mould can enter the food system

zearalenone, ochratoxin A and patulin. And many countries now have legislated maximum levels of these toxins allowed in food.

A characteristic of mycotoxin contamination is that it is not uniformly spread throughout an agricultural product. This means that specific sampling methods for each different product and toxin combination are needed.

A wide range of analytical methods have been developed for detecting mycotoxins in food. All these methods – apart from near-infrared – require extraction of the toxin from the food, using polar solvent mixtures, prior to analysis. These extracts, which still contain many soluble food compounds, can be analysed directly in enzyme-linked immunosorbent assays (ELISAs) or applied to a variety of screening methods such as lateral flow devices, dipsticks and biosensors. These methodologies all rely on the use of mycotoxin-

specific antibodies to discriminate the mycotoxin from the coextracted food components and generally give semi-quantitative results.

For more accurate determination of mycotoxins, the extracts require purifying. The clean-up method of choice is solid phase extraction, where the mycotoxin binds to the sorbent, the impurities are washed through the column and finally the mycotoxin is released. Also popular are multifunctional columns – packed with adsorbent mixtures such as alumina and charcoal – that absorb the impurities as the mycotoxin extract passes through.

After extract clean-up, mycotoxins can be analysed by thin-layer, gas or high-performance liquid chromatography. This last method coupled with ultraviolet, fluorescence or mass spectrometric detection is the most frequently used analysis technique. The use of tandem mass spectrometric detection here can provide multitoxin analysis combined with confirmatory evidence within the same experiment. Multitoxin analysis is useful for foods that can be contaminated by a number of different mycotoxins, produced by the same or different fungal species.

Interpretation of ancient writings suggests that mycotoxins have caused health problems since the earliest times of recorded history. And unless we can inhibit the toxin synthetic capability of the mycotoxin-producing fungi, we shall need to continue to tap into the advances in analytical chemistry to monitor these potent natural toxins.

Read Gordon Seymour Shephard's tutorial review 'Determination of mycotoxins in human foods' in issue 11, 2008 of Chemical Society Reviews

Reference
G S Shephard, *Chem. Soc. Rev.*, 2008, DOI: 10.1039/b713084h

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Chemistry is the business

A V Rama Rao talks to Joanne Thomson about how science has shaped development in India



A V Rama Rao

A V Rama Rao is founder and managing director of Avra Laboratories in Hyderabad, India, a research-focused company that caters to the process and product needs of the pharmaceutical industry. He has published more than two hundred and fifty papers on the isolation, structural elucidation and synthesis of natural products and has developed more than fifty drug technologies commercialised by the pharmaceutical industry.

What inspired you to become a scientist?

The science of natural products fascinated me in my early days. I was surrounded by inspiration. I lived close to poppy fields – my grandfather was addicted to the morphine made from them to relieve his knee pains. Malaria was common and I used to take quinine tablets whenever I suffered from it. I was also fascinated to see fabrics dyed with natural colours, especially indigo, which was cultivated in India.

What was your big break?

My two year stint with E J Corey at Harvard University. There I realised the importance in choosing the right product for synthesis. I also realised that the product should have some relevance to society. I returned to India to work at the National Chemical Laboratory (NCL) in 1977. Most of my senior colleagues at NCL discouraged me from taking on challenging synthetic projects as the institute (albeit a premier one) was not well equipped and it took months to import reagents at the time (the early 1980s). In spite of all these hurdles, I was always keen on tackling such fascinating projects.

You founded Avra Laboratories in 1995. What were your motivations, and what are your aspirations for the company for the years ahead?

When I retired as director of the Indian Institute of Chemical Technology in 1995, I wanted an exciting and viable alternative. I decided not to accept a distinguished scientist position at the Council for Scientific and Industrial Research because normally, such distinguished persons feel more like extinguished entities within the organisation. I decided to utilise my scientific expertise to tackle some industrial projects. Most people become consultants as it is an easy option. I wanted to offer more than paper solutions; I wanted to have a lab where I could work with a team of scientists and provide real solutions on a fee for service model. This idea led to the genesis of Avra Laboratories.

In the future, we would like to align with some of the big pharma companies and offer our R&D services on a long-term basis.

Your sons, Ramakrishna and Chandra, both work at Avra. How important is it to you to maintain these family connections in business?

For a medium-sized industry like us, I feel it is better to be run by family, provided that they are well qualified to lead the team. Ramakrishna has a Master's degree in industrial chemistry and an MBA. He meticulously plans the commercial operations. Chandra obtained a PhD in organic chemistry from Cambridge University. He is a very good communicator and inspires young R&D personnel in Avra. All three of us have defined roles and operate professionally.

India is becoming a major player in chemical research. How important do you think chemistry is to the future development of India?

Since we joined the World Trade Organisation, the Indian pharma industry has been rapidly expanding and now employs even expats in top R&D positions. During the last three years, many international pharma companies have started R&D divisions in India and the government has doubled the R&D budget for public institutions.

I believe India is among the few developing nations that can boast of an indigenous but globally respected chemical industry. India thus has an established platform to enable it to gain further stature as a hub for manufacturing and innovation by taking advantage of the lower costs and abundant talent.

The generic market has always been the mainstay of the Indian pharmaceutical industry but competition has increased greatly in recent years. What strategies should companies adopt in the coming years to survive?

Competition is good for the consumer and puts pressure on manufacturers to innovate and bring in efficiencies of scale. If you cannot beat your competitor, the other option would be to join him. I believe there will be consolidation in the Indian chemical space with mergers and acquisitions. The pressure to survive might kindle innovating strategies that could cater to an unmet need at the time.

Essential elements

Good prospects for *Lab on a Chip*

Lab on a Chip, the miniaturisation journal for chemistry, biology and bioengineering is now taking miniaturisation science to the next level. With journal submissions steeply rising over the past years, 2009 will see the journal increase in frequency to 24 issues per year. The new year will also herald the arrival of George Whitesides as the new editorial board chair of *Lab on a Chip*. 'There is no one in the field who is better equipped than Professor Whitesides to help *Lab on a Chip* ascend to the next level in terms of quality, visibility and impact,' comments Harp Minhas, editor of *Lab on a Chip*.

Lab on a Chip has established itself at the heart of the miniaturisation community through various sponsorships for prizes and awards, which recognise and highlight the contributions of young and emerging scientists in the field, to



George Whitesides, the new editorial board chair of *Lab on a Chip*

online support via new initiatives such as 'Chips & Tips' - the quick-fix online forum providing useful advice on common practical problems for scientists in the miniaturisation world.

More issues, more leading research and a new editorial board chair – 2009 promises to be an exciting year for the *Lab on a Chip* community.

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ChemComm in Korea

The Second *ChemComm* International Symposium on Supramolecular Chemistry will take place in Korea in November 2008 with one-day meetings in Seoul, Daejeon and Pohang. This follows a successful First *ChemComm* International Symposium on Polymers and Polymer Science in China in December 2007.

ChemComm, with an impact factor of 5.14, publishes some of the most significant work in the chemical sciences and is

the fastest at publishing general chemistry communications.

ChemComm Symposia aim to bring together scientists in an environment that fosters collaborations between the researchers and universities involved. All symposia are free to attend and each is devoted to a topical area of the chemical



sciences, featuring an invited programme of international and locally-based expert speakers.

In this second symposium, the programme is supplemented by a poster session, showcasing the work of local universities.

As the second symposium approaches fast and promises to be as successful as the first, plans for a third symposium

next year in China are already well underway. The Third *ChemComm* International Symposium on the topic of Organic Chemistry will be held in February 2009, with meetings in Beijing, Shanghai and Chengdu.

For more details on *ChemComm* Symposia, and full programme schedules for the Second Symposium on Supramolecular Chemistry in Korea, visit www.rsc.org/chemcommsymposia.

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