Organic & Biomolecular Chemistry

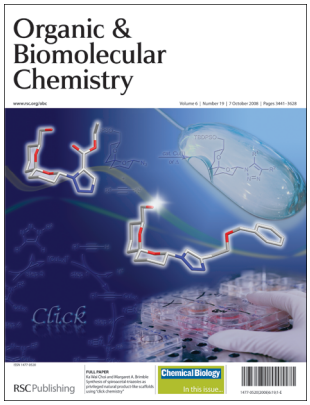
An international journal of synthetic, physical and biomolecular organic chemistry

www.rsc.org/obc

RSC Publishing is a not-for-profit publisher and a division of the Royal Society of Chemistry. Any surplus made is used to support charitable activities aimed at advancing the chemical sciences. Full details are available from www.rsc.org

IN THIS ISSUE

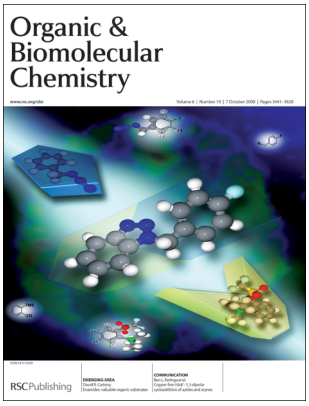
ISSN 1477-0520 CODEN OBCRAK 6(19) 3441–3628 (2008)



Cover

See Margaret A. Brimble *et al.*, pp. 3518–3526.
The efficient "click chemistry" has been used to elaborate a spiroacetal skeleton to incorporate a triazole unit. The copper-mediated catalytic cycle is summarised in the bottom left corner.

Image reproduced by permission of Ka Wai Choi and Margaret A. Brimble from *Organic & Biomolecular Chemistry*, 2008, **6**, 3518.



Inside cover

See Ben L. Feringa *et al.*, pp. 3461–3463.
An artist's impression of an azide and an aryne merging together in a new metal-free click reaction that has potential for the introduction of radioactive labels for biomedical imaging.

Image reproduced by permission of Ben Feringa from *Organic & Biomolecular Chemistry*, 2008, **6**, 3461.

CHEMICAL BIOLOGY

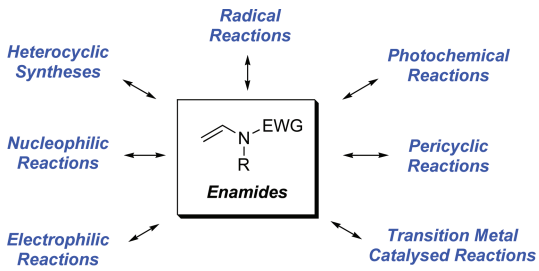
Drawing together research highlights and news from all RSC publications, *Chemical Biology* provides a 'snapshot' of the latest developments in chemical biology, showcasing newsworthy articles and significant scientific advances.

Chemical Biology

October 2008/Volume 3/Issue 10

www.rsc.org/chembiology

EMERGING AREA



The Chemistry of Enamides

Organic & Biomolecular Chemistry

An international journal of synthetic, physical and biomolecular organic chemistry

www.rsc.org/obc

Organic & Biomolecular Chemistry brings together molecular design, synthesis, structure, function and reactivity in one journal. It publishes fundamental work on synthetic, physical and biomolecular organic chemistry as well as all organic aspects of: chemical biology, medicinal chemistry, natural product chemistry, supramolecular chemistry, macromolecular chemistry, theoretical chemistry, and catalysis.

Organic & Biomolecular Chemistry (print: ISSN 1477-0520; electronic: ISSN 1477-0539) is published 24 times a year by the Royal Society of Chemistry, Thomas Graham House, Science Park, Milton Road, Cambridge, UK CB4 0WF.

All orders, with cheques made payable to the Royal Society of Chemistry, should be sent to RSC Distribution Services, c/o Portland Customer Services, Commerce Way, Colchester, Essex, UK CO2 8HP. Tel +44 (0) 1206 226050; E-mail sales@rscdistribution.org

2008 Annual (print + electronic) subscription price: £2725; US$5423. 2008 Annual (electronic) subscription price: £2453; US$4881. Customers in Canada will be subject to a surcharge to cover GST. Customers in the EU subscribing to the electronic version only will be charged VAT.

If you take an institutional subscription to any RSC journal you are entitled to free, site-wide web access to that journal. You can arrange access *via* Internet Protocol (IP) address at www. rsc.org/ip. Customers should make payments by cheque in sterling payable on a UK clearing bank or in US dollars payable on a US clearing bank. Periodicals postage paid at Rahway, NJ, USA, and at additional mailing offices. Airfreight and mailing in the USA by Mercury Airfreight International Ltd., 365 Blair Road, Avenel, NJ 07001, USA.

US Postmaster: send address changes to Organic & Biomolecular Chemistry, c/o Mercury Airfreight International Ltd., 365 Blair Road, Avenel, NJ 07001. All despatches outside the UK by Consolidated Airfreight.

PRINTED IN THE UK

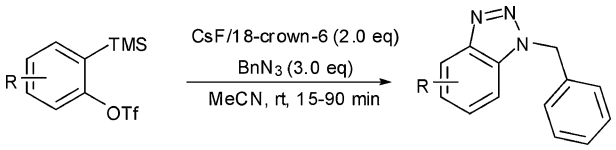
Advertisement sales: Tel +44 (0) 1223 432246; Fax +44 (0) 1223 426017; E-mail advertising@rsc.org

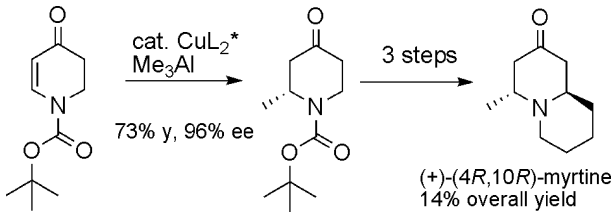
INFORMATION FOR AUTHORS

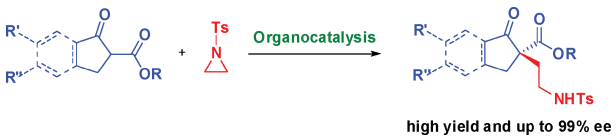
Full details of how to submit material for publication in Organic & Biomolecular Chemistry are given in the Instructions for Authors (available from http://www.rsc.org/authors). Submissions should be sent *via* ReSourCe: http://www.rsc.org/resource

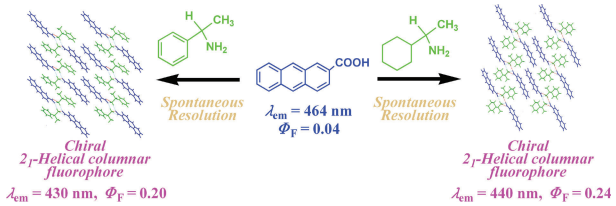
The paper used in this publication meets the requirements of ANSI/NISO Z39.48-1992 (Permanence of Paper).

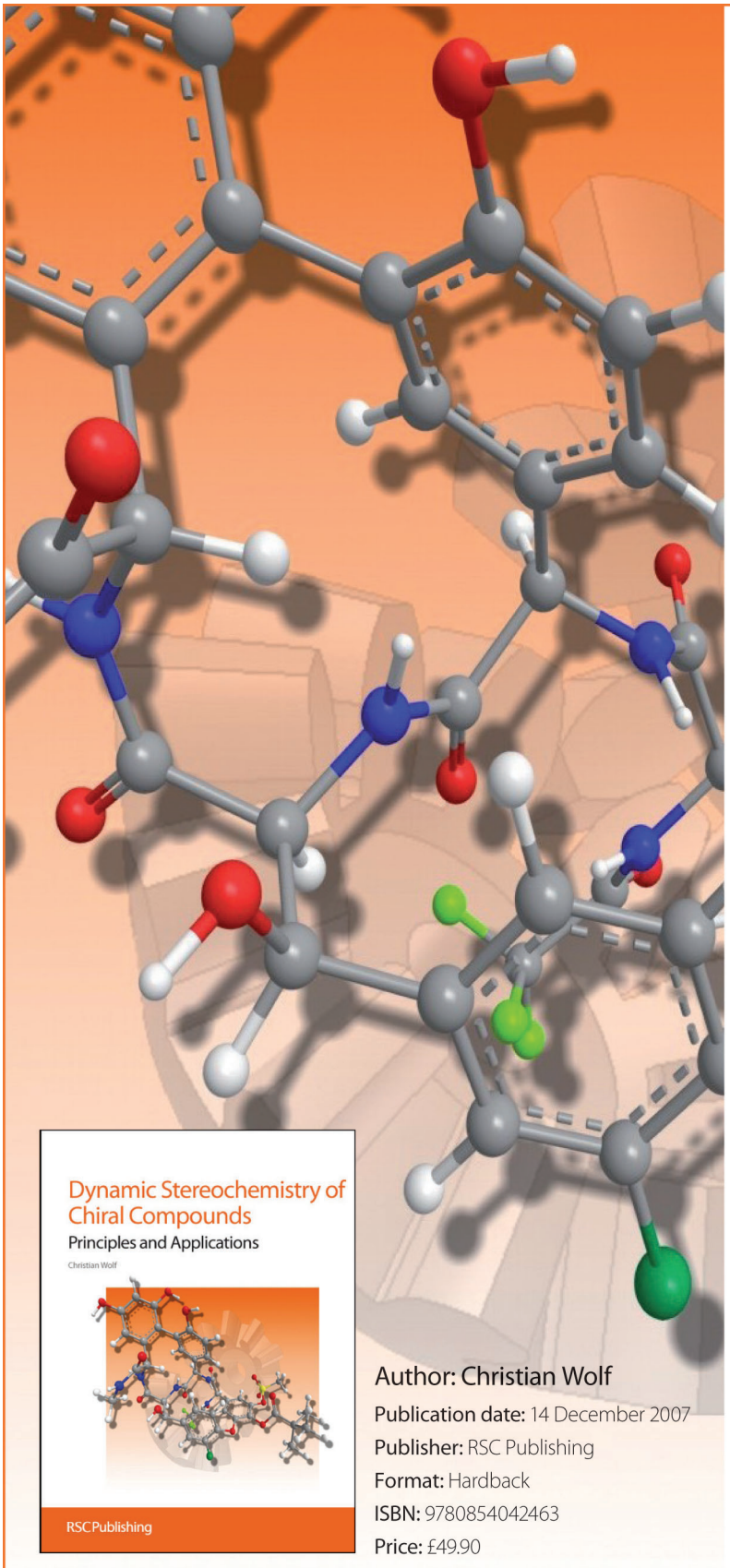
Royal Society of Chemistry: Registered Charity No. 207890











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

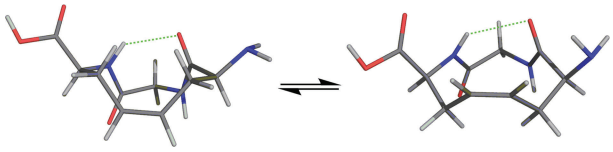
This book will be of particular interest to advanced undergraduates, graduates and professionals working and researching in the fields of synthetic organic chemistry and stereochemistry.

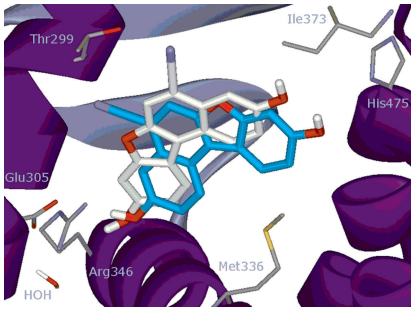
Author: Christian Wolf
Publication date: 14 December 2007
Publisher: RSC Publishing
Format: Hardback
ISBN: 9780854042463
Price: £49.90

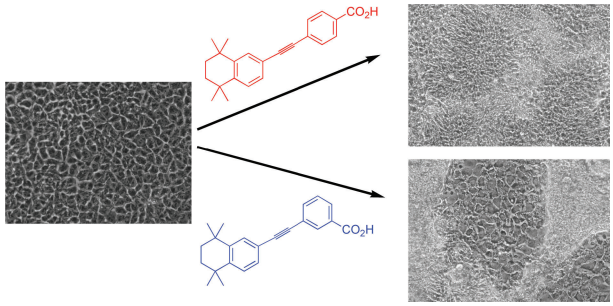
030804

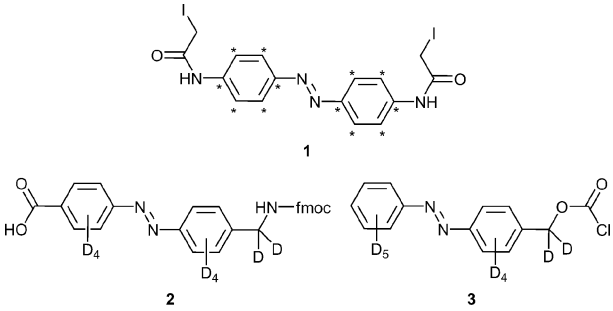
RSC Publishing

www.rsc.org/books









42nd IUPAC CONGRESS Chemistry Solutions

2–7 August 2009 | SECC | Glasgow | Scotland | UK

On behalf of IUPAC, the RSC is delighted to host the 42nd Congress (IUPAC 2009), the history of which goes back to 1894. RSC and IUPAC members, groups and networks have contributed a wealth of ideas to make this the biggest UK chemistry conference for several years.

As well as a programme including more than 50 symposia, a large poster session and a scientific exhibition, we are planning a series of social and satellite events to enhance networking and discussion opportunities.

Sponsored by Schering-Plough

Call for abstracts

This is your chance to take part in IUPAC 2009. Contributions are invited for oral presentation by 16 January 2009 and poster abstracts are welcome until 5 June 2009.

Themes

- Analysis & Detection
- Chemistry for Health
- Communication & Education
- Energy & Environment
- Industry & Innovation
- Materials
- Synthesis & Mechanisms

Plenary speakers

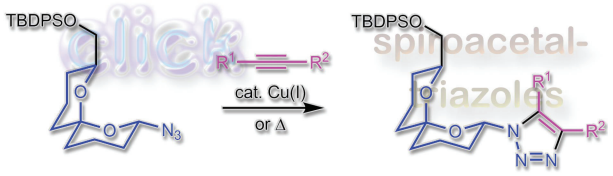
Peter G Bruce, University of St Andrews
Chris Dobson, University of Cambridge
Ben L Feringa, University of Groningen
Sir Harold Kroto, Florida State University
Klaus Müllen, Max-Planck Institute for Polymer Research
Sir J Fraser Stoddart, Northwestern University
Vivian W W Yam, The University of Hong Kong
Richard N Zare, Stanford University

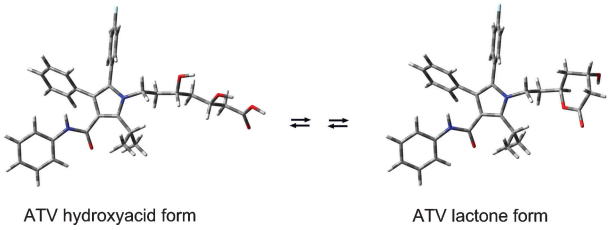
For a detailed list of symposia, keynote speakers and to submit an abstract visit our website.

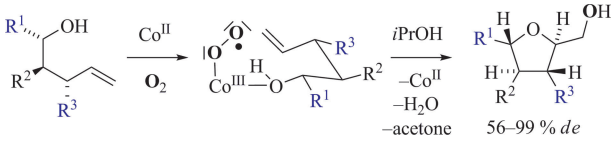
RSC | Advancing the Chemical Sciences

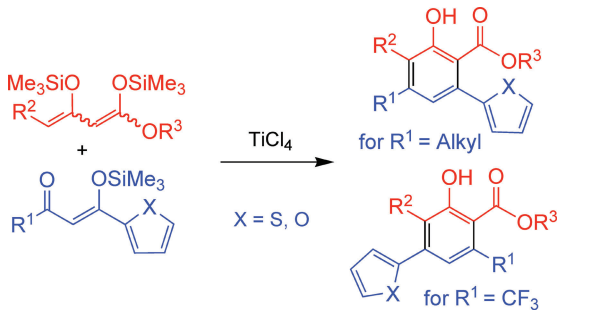
www.iupac2009.org

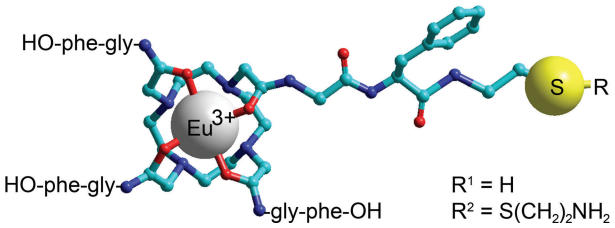
Registered Charity Number 207890

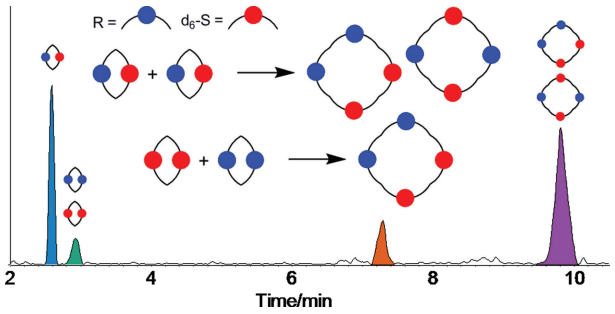


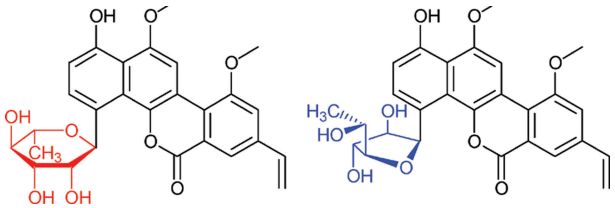


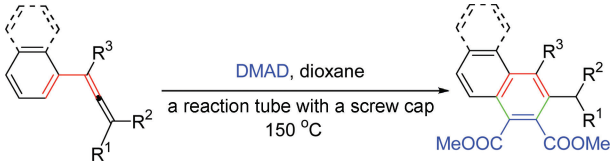


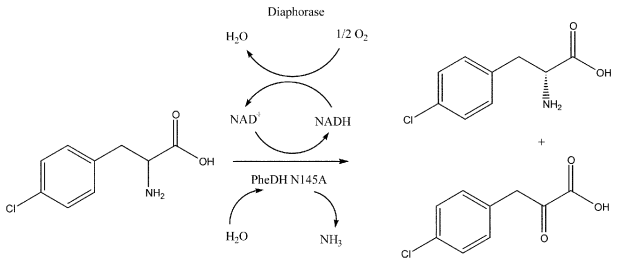


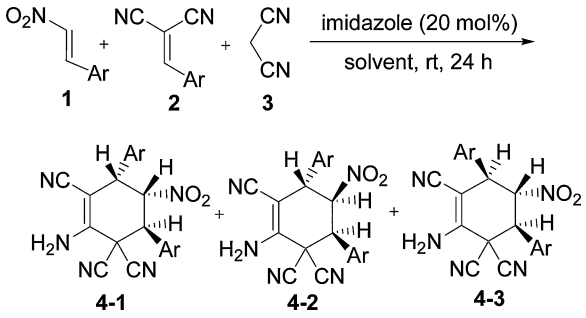


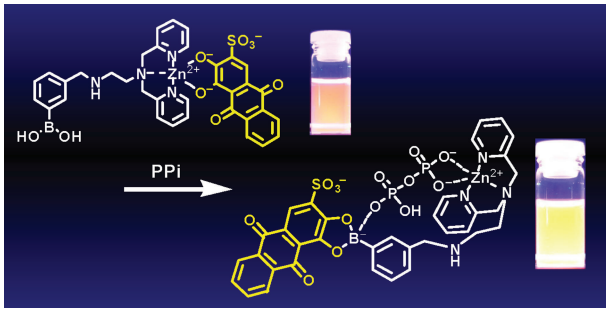




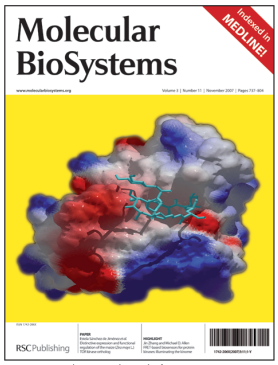








It's official, *Molecular BioSystems* has separated from host journal, *Chemical Communications*, and is now a fully fledged solo publication. Its availability since launch to readers of *Chemical Communications* and the online hosts, *Organic & Biomolecular Chemistry*, *Lab on a Chip*, *The Analyst* and *Analytical Abstracts* has ensured that *Molecular BioSystems* received a large and interdisciplinary audience from the outset. *Organic & Biomolecular Chemistry* readers wishing to continue to read *Molecular BioSystems* now need to recommend the journal to their librarian. Fill in the online recommendation form at www.rsc.org/libraryrecommendation



www.molecularbiosystems.org

AUTHOR INDEX

FREE E-MAIL ALERTS AND RSS FEEDS

Contents lists in advance of publication are available on the web *via* www.rsc.org/obc – or take advantage of our free e-mail alerting service (www.rsc.org/ej_alert) to receive notification each time a new list becomes available.

Try our RSS feeds for up-to-the-minute news of the latest research. By setting up RSS feeds, preferably using feed reader software, you can be alerted to the latest Advance Articles published on the RSC web site. Visit www.rsc.org/publishing/technology/rss.asp for details.

ADVANCE ARTICLES AND ELECTRONIC JOURNAL

Free site-wide access to Advance Articles and the electronic form of this journal is provided with a full-rate institutional subscription. See www.rsc.org/ejs for more information.

* Indicates the author for correspondence: see article for details.

Electronic supplementary information (ESI) is available *via* the online article (see http://www.rsc.org/esi for general information about ESI).

October 2008 / Volume 3 / Issue 10 / ISSN 1747-1605 / CBHIBN / www.rsc.org/chembiology

Chemical Biology

Synthetic lesions added to DNA to probe its stability

Discovering the secrets of DNA repair

A modified DNA is helping scientists to understand the sophisticated DNA repair mechanisms that allow dormant bacteria to come 'back to life'.

Thomas Carell and Eva Bürckstümmer at the Ludwig Maximilian University of Munich, Germany, have made short DNA strands containing lesions. Carell explains that this is the key to understanding DNA repair. 'So far any study of this enigmatic process has been hampered by a lack of DNA containing this lesion,' he explains.

The lesions are analogues of those triggered when UV light acts on DNA stored in spores such as the *Bacillus* bacteria spore. In nature, these spores can lie dormant for many years, storing DNA, but then return to life, explains Carell. How spores store DNA and how lesion repair occurs are the questions the German duo would like to answer.

Carell and Bürckstümmer made their DNA strands by synthesising two isomers of a dinucleotide lesion analogue and incorporating them into DNA. They found that one DNA was more stable than the other, suggesting that the natural lesion could have a similar structure to the analogue in the more stable DNA. Carell points out that similar lesion analogues are substrates for the spore DNA repair enzyme so that the new strands could help further studies into the enzyme mechanism.

ISTOCKPHOTOS

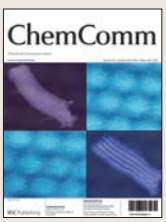
Fixing damaged DNA: if only it were this simple...

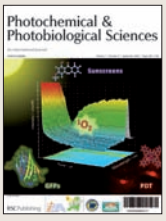
Glen Burley, an expert in DNA nanotechnology at the University of Leicester, UK, says that the work is exciting as it provides a method for investigating how spores repair damaged DNA. 'This is a compelling question as DNA damage processes in spores differ from those in mammals,' he says. 'These methods would likely lead to a greater understanding of how spores can survive for long periods and in hostile conditions – for example hot springs.'

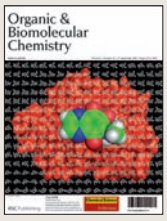
Carell explains that although the repair process in the spore is unique, lesion recognition by enzymes is more general. 'Such enzymes are also operating in our cells,' he says, 'so a deeper understanding of this class of enzymes is desperately needed.' Carell adds that he is particularly interested in learning more about failures in repair. 'These are responsible for mutations which in turn lead to dangerous cellular situations which might produce cancer,' he says. *Katherine Davies*

Reference
E Bürckstümmer and T Carell, *Chem. Commun.*, 2008, 4037 (DOI: 10.1039/b810008j)

In this issue







Research highlights

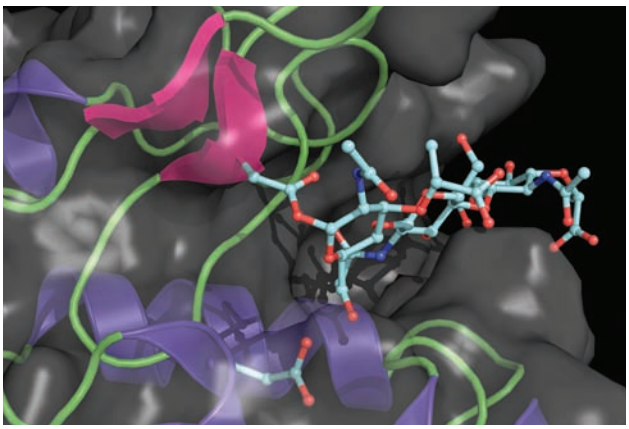
Calculations validate alternative to much-published enzyme mechanism

Rewriting the biochemistry textbooks...

Hen egg white lysozyme is a common example in textbooks discussing enzyme mechanism. But now scientists from the University of Bristol, UK, have used molecular dynamics simulations to show that the traditional mechanism is wrong. 'The textbooks need to be rewritten,' says researcher Adrian Mulholland, who led the team behind the work.

Lysozymes break down polysaccharides in bacterial cell walls, and so play a role in defence against pathogens. The textbook mechanism of hen egg white lysozyme proceeds through an intermediate in which a sugar ring on the substrate interacts ionically with the enzyme. In the revised mechanism the bond is covalent.

'Knowing how reaction intermediates form is central to understanding why enzymes are such efficient catalysts,' says Mulholland. 'This sort of detailed knowledge is also important in designing enzyme inhibitors as drugs,' he adds.



The hen egg white lysozyme mechanism proceeds through a covalent intermediate

Reference
A L Bowman I M Grant and A J Mulholland, *Chem. Commun.*, 2008, DOI: 10.1039/b810099c

A covalent intermediate has been suggested previously, clarifies Mulholland. But the experimental work that led to this proposal relied on modified enzymes and substrates because the wild type enzyme is too efficient for any intermediate to be detected. 'Some people have suggested that the experiments were not relevant to the real target,' Mulholland says.

Mulholland's computational model is based on the wild type enzyme and substrate. Moreover it includes the entire protein as well as its water environment, in contrast to previous smaller models. The evidence from the modelling and the experiments together is enough to confirm the revised mechanism, says Mulholland.

Stephen Withers was involved in the experimental research on hen egg white lysozyme, and is pleased that Mulholland's calculations have confirmed the revised mechanism. The scientist from the University of British Columbia in Vancouver, Canada, welcomes the development of computational studies to supplement experiments. 'It is simply not possible to experimentally probe all proteins,' he says. 'We shall rely on computational approaches increasingly to guide our choice of systems to study experimentally.' *Danièle Gibney*

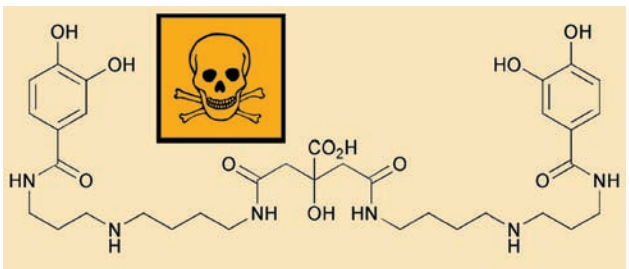
Enzyme study reveals details of potential target in the fight against anthrax

... and revising route to stealthy siderophore

A surprising result has led UK scientists to revise the proposed biosynthetic route to petrobactin – a molecule needed by anthrax-causing bacteria to replicate. Greg Challis at the University of Warwick and colleagues say that their findings may ultimately lead to the development of new antibiotics for the disease.

Petrobactin is an iron scavenger secreted by *Bacillus anthracis* to collect the iron it needs to reproduce. Called a stealth siderophore, it evades the molecule our immune system produces to capture it, contributing to the organism's virulence.

Challis's group has examined the role of the enzyme AsbB in petrobactin's biosynthesis. They first identified possible substrates for AsbB and obtained pure enzyme. Then, by treating the enzyme with different substrate combinations and finding which led to products and how quickly, the researchers



Petrobactin – the stealth iron scavenger of *Bacillus anthracis*

Reference
D Oves-Costales *et al*, *Chem. Commun.*, 2008, 4034 (DOI: 10.1039/b809353a)

showed that a previously proposed intermediate is unlikely to be significant in the pathway.

Challis says that he and his team were surprised by the findings, which led them to suggest a revised pathway to petrobactin. They had assumed, based on studies of other siderophore biosynthetic pathways, that the route would be significantly different from the one they now propose.

'Our results provide the basic biochemical knowledge required to screen for inhibitors of AsbB,' says Challis. This could lead to inhibitors for petrobactin biosynthesis and so a potential anthrax treatment, he adds.

The team's results also confirmed earlier computational predictions that enzymes such as AsbB use particular citrate derivatives as substrates, something that Christopher Schofield who investigates biosynthetic enzymes at the University of Oxford, UK, finds interesting. He says that the work 'provides more evidence for the value of chemical insights into bioinformatic analyses' and agrees that it could also one day help provide new antibacterials.

Challis and group member Daniel Oves-Costales were recently awarded a Biotechnology and Biological Sciences Research Council (BBSRC) grant to continue investigating the mechanisms of petrobactin biosynthesis and to search for inhibitors. *Frances Galvin*

Spectroscopic techniques combined for easier metabolomic analysis

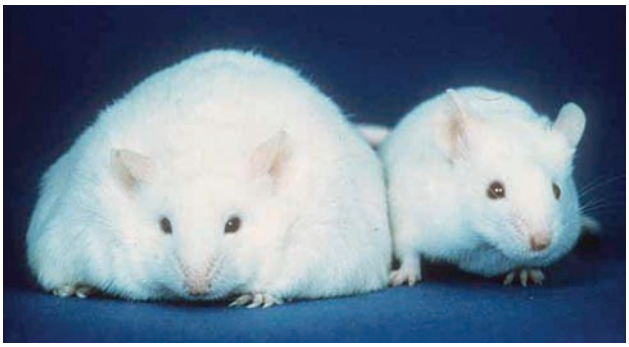
Metabolic markers for diabetes

ONRL

Finding how a trace molecule's concentration varies when it's mixed in a jumble of others is not straightforward but this is just what a metabolomics scientist does every day. Now an international team is combining several analytical techniques to make the process easier and applying its method to study diabetes.

Metabolomics is the study of metabolites – the small molecules formed by specific processes inside a single cell. As variations in levels of some of these may be linked to metabolic disorders such as diabetes, identifying these so-called metabolic markers has the potential to provide diagnostic information and to lead to better therapies.

With this in mind, Geoffrey Gipson at Drexel University, Philadelphia, US, and colleagues in the US and UK, combined spectroscopic methods such as nuclear magnetic resonance (NMR) and liquid chromatography-mass spectrometry (LC-MS) to analyse the metabolites in urine and tissue samples from mice deficient in the hormone protein leptin. Leptin has a key role in regulating metabolism and the leptin-deficient mice display several genetic traits associated with type 2 diabetes. By comparing the metabolite levels with those in control mice, the researchers confirmed that many pathways, including fatty acid metabolism, are altered in 'diabetic' mice. Gipson says that these pathways could potentially be targeted for diabetes treatments.



Leptin-deficient mice (left) show genetic traits associated with diabetes and obesity

Reference
G T Gipson *et al*, *Mol. BioSyst.*, 2008, **4**, 1015 (DOI: 10.1039/b807332e)

While Gipson admits that there are limitations in using animals to model human conditions, he explains that metabolism is a fundamental biological process which has been highly conserved over evolutionary time. 'As such, there are many cross-species molecular similarities which allow researchers to gain critical insights into human disease,' he adds. Given this, the biggest challenge, says Gipson, is in applying the new knowledge gained through metabolic profiling research into therapies for patients living with diabetes.

Jules Griffin, an expert in metabolomics at the University of Cambridge, UK, commends the team's integrated approach. 'While NMR has been used widely in mammalian disease models,' says Griffin, 'the use of LC-MS based approaches has lagged behind, in part because of the greater challenges in technical reproducibility. By picking a well-characterised model of type 2 diabetes the team has been able to validate its approach and then extend its analysis to new metabolite changes not previously described.'

Kathleen Too

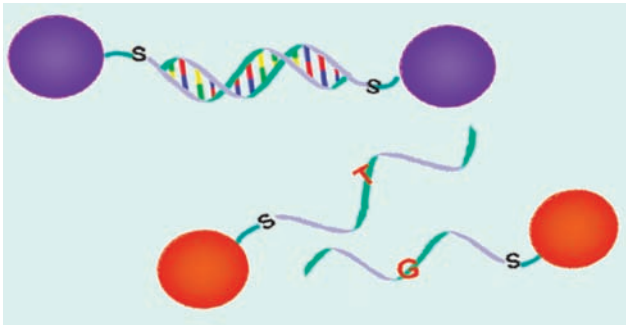
Protein maintains activity at high temperature to identify nucleotide differences

Mismatched DNA analysis by eye

A colourful approach to detecting DNA variations can take the heat. A team led by Changill Ban from Pohang University of Science and Technology and Min Su Han from Chuang-Ang University, Seoul, in South Korea, has tested a technique that reveals mismatched DNA base pairs by a temperature change.

The team's method detects DNA in which one base is paired with any base that is not its complementary partner. Mismatch detection can be used to find single base differences called single nucleotide polymorphisms (SNPs). Rapid SNP detection is essential, says Ban, as these DNA variations can be a marker for genetic disease.

The team bound gold nanoparticles to single stranded DNA which then pairs to form duplex DNA containing mismatches. As the DNA pairs, the system turns from red to purple as the nanoparticles aggregate. On heating, the system reverts to red as the strands unpair or 'melt'. The researchers observed that the colour change occurs at a higher temperature when the system is treated with MutS, a protein that binds selectively to mismatched pairs. They also found that complexes containing different DNA mismatches melt at different temperatures, so it is possible to identify which bases are mismatched.



When gold-bound DNA strands unpair the system changes from purple (top) to red (bottom) as the gold de-aggregates

Reference
M Cho, M S Han and C Ban, *Chem. Commun.*, 2008, DOI: 10.1039/b811346g

Ban says that, as a colorimetric assay, the system is 'simpler and more convenient than other methods, allowing detection with the naked eye.' Most current colorimetric detection methods rely on enzyme activity, requiring physiological conditions to work. By using MutS, the team avoids this limitation, as the protein maintains its activity under a range of pHs and at high temperatures.

The next stage will be to adapt the method for microarray technology, says Ban, allowing high throughput screening of DNA samples.

Harriet Brewerton

Versatile protein synthesis optimised to make biologically active target

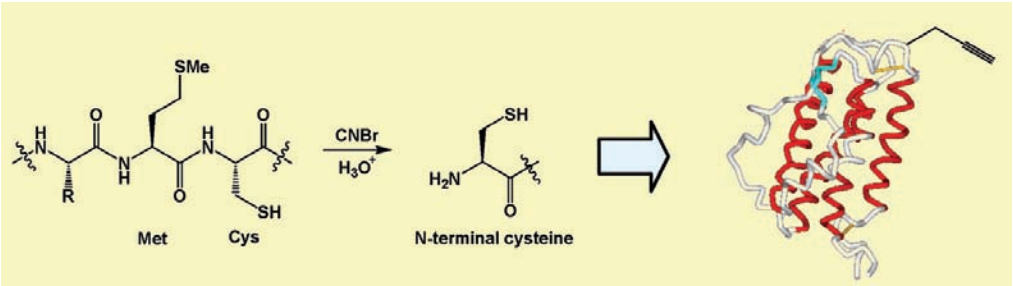
Mix and match protein building blocks

An improved procedure for breaking proteins in two is allowing chemists to create new proteins. Derek Macmillan and Jonathan Richardson from University College London, UK, have used their method to make a biologically active protein.

Low reaction yields make creating large proteins by chemical synthesis unfeasible, yet not all proteins can be prepared easily by other routes. Native chemical ligation (NCL) is one technique that chemists can use to create these proteins by joining a small peptide containing a thioester to a protein fragment with an N-terminal cysteine. In this way troublesome proteins can be created without having to synthesise the whole protein from scratch.

The advantages of NCL are its 'versatility and reliability', explains Macmillan. 'The reaction is conducted in aqueous solution with no protecting groups, and the product has a native peptide bond,' he adds.

But whilst the small peptides required for NCL can be made by peptide synthesis, preparing the large protein fragment is often more problematic and poses many of the same problems associated with creating whole proteins. Now, Macmillan and Richardson have optimised their procedure for generating these fragments. The starting, bacterially-derived protein is cleaved next to a methionine to give two fragments, one with the cysteine at its N-terminus. The cysteine-containing fragment is then isolated and combined with a synthetic peptide containing a thioester to create a whole, semi-synthetic protein.



Cyanogen bromide is used to cleave a protein next to a methionine residue to give a protein fragment for NCL

Using their optimised procedure Macmillan and Richardson were able to create a biologically active variant of erythropoietin, a hormone protein involved in red blood cell production which is used in the treatment of anaemia. Commenting on this success, Phil Dawson an expert in synthetic protein chemistry at The Scripps Research Institute, La Jolla, US, says that 'the functional complexity of large proteins can turn even the most straightforward procedure into a daunting challenge. The Macmillan lab has taken an important first step towards establishing a robust semi-synthesis for an important therapeutic target.'

Russell Johnson

Reference

J P Richardson and D Macmillan, *Org. Biomol. Chem.*, 2008, DOI: 10.1039/b811501j

In the current issue of Research Articles...

Targeting transcription factors for therapeutic benefit
Paul Brennan *et al*, *Mol. BioSyst.*, 2008, **4**, 909 (DOI: 10.1039/b801920g)

Immunotherapy: a way to improve the therapeutic outcome of photodynamic therapy?
Mateusz Kwitniewski *et al*, *Photochem. Photobiol. Sci.*, 2008, **7**, 1011 (DOI: 10.1039/b806710d)

Open micro-fluidic system for atomic force microscopy-guided in situ electrochemical probing of a single cell
WonHyoung Ryu *et al*, *Lab Chip*, 2008, **8**, 1460 (DOI: 10.1039/b803450h)

Integrated GC–MS and LC–MS plasma metabonomics analysis of ankylosing spondylitis
Peng Gao *et al*, *Analyst*, 2008, **133**, 1214 (DOI: 10.1039/b807369d)

Transcription monitoring using fused RNA with a dye-binding light-up aptamer as a tag: a blue fluorescent RNA
Shinsuke Sando *et al*, *Chem. Commun.*, 2008, 3858 (DOI: 10.1039/b808449a)

Imaging of essential and toxic elements in biological tissues by LA-ICP-MS
J Sabine Becker *et al*, *J. Anal. At. Spectrom.*, 2008, **23**, 1275 (DOI: 10.1039/b805228j)

Protein modification for single molecule fluorescence microscopy
Mark S Dillingham and Mark I Wallace, *Org. Biomol. Chem.*, 2008, **6**, 3031 (DOI: 10.1039/b808552h)

The use of gold nanoparticles in diagnostics and detection
Robert Wilson, *Chem. Soc. Rev.*, 2008, **37**, 2028 (DOI: 10.1039/b712179m)

Modeling the reactive properties of tandemly activated tRNAs
Maria Duca *et al*, *Org. Biomol. Chem.*, 2008, **6**, 3292 (DOI: 10.1039/b806790b)

Probing (macro)molecular transport through cell walls
Giona Kilcher *et al*, *Faraday Discuss.*, 2008, **139**, 199 (DOI: 10.1039/b717840a)

Read more at www.rsc.org/chembiology

Interview

Mapping out success

OBC lecture award winner, Akimitsu Okamoto, talks about chemical probes and daydreaming over maps. Vikki Allen meets him in Pittsburgh to find out more

Akimitsu Okamoto

Akimitsu Okamoto is leader of the Okamoto Initiative Research Unit at RIKEN Advanced Science Institute. He is the 2008 recipient of the *Organic & Biomolecular Chemistry* lecture award. His primary research interests focus on the design and synthesis of biopolymers, and recognising and visualising single components or atoms in biopolymers.

What inspired you to become a chemist?
I grew up with many empty chemical boxes around the house. My father used to work in a trading company that handled chemicals for the porcelain and chinaware that Nagoya is known for and he used to bring the empty boxes home. I became interested in these boxes; I wanted to know what had been inside them, and what the chemicals had looked like.

What motivated you to specialise in bioorganic/biological chemistry?
I started out in graduate school in synthetic organic chemistry, working on natural products, so I made many compounds. Such compounds are often used in biotechnology. Choosing biological chemistry wasn't a conscious decision. The department that I studied at was very small and gave a good basic range of courses, but I found the 'bio' courses the most interesting and they introduced me to DNA. Bioorganic chemistry sounds good, too! And bioorganic chemistry is such an important field, bridging chemistry and biology. Since then, my research has changed gradually towards biological chemistry.

I began my independent career nine years ago, initially in collaboration with Professor Isao Saito, who worked at Kyoto University at the time. The projects that we started then led me into the research that I now do.

What hot project are you working on at the moment?
I want to see living cells working. I want to see DNA and RNA working. So in my laboratory, we make lots of nucleic acid probes – fluorescent probes, chemical probes. There are a number of protein probes but we don't yet have any really good methods to look at RNA and DNA.

We are working on a number of projects to look at living cells – stem cells – and are trying to understand the mechanism by which they work. What is it that causes them to live, and to become skin or hair? What is the 'life' in these cells? What roles do RNA and DNA play? It's quite a fundamental project.

What do you love most about your job?
I enjoy my job. There is a lot of work to do in the DNA and RNA field using our chemical probes. The probes work really well, so I like to know that we can use our probes to look at problems and that they are well designed.

You are this year's recipient of the *OBC* lecture award. How do you feel about the award?
I'm happy, very happy. Of course it is good to know that my work has been appreciated. I would very much like to thank my collaborators and laboratory co-workers. The topic of my award lecture will focus on one particular example of the work we do looking at the use of osmium to investigate cells. It's very interesting.

Which scientist from the past would you most like to meet and why?
This is a really difficult question. I respect all scientists that are dedicated and work hard every day, those who try. Whether you get a really good result depends on if you are lucky or not. I would not be able to choose just one person in particular.

What do you do when you are not working?
I like going to book stores. And I really love maps. I don't have enough time to travel, so I like to read the maps of places that I would like to visit instead. I always buy maps when I do get to travel. Last week, I was giving talks in the Czech Republic and so I bought a country map. I also recently went to Mexico and have a Mexican map too.

I particularly like the world map. Czech maps and Spanish maps show you the language differences and reflect the different cultures of countries. Sometimes, maps can be funny too. I have an Australian world map that is upside down. The south is at the top of the map and north towards the bottom. I think it's a special map though!

I would love to visit everywhere, but my first ever foreign holiday was to the UK when I was a graduate and I would love to go back. I visited London and Stonehenge.

And finally, if you weren't a scientist what would you be?
When I was an undergraduate, I got a licence to act as a travel agent in Japan. I wanted to be a tour organiser and travel around with groups of people exploring places. I like planning travel, but then I started going into the chemical labs every day and just didn't have the time to do this as well. So, if I didn't do chemistry I would be a tour operator.

Instant insight

Nature's fruitful chemistry

Bernhard Kräutler and Thomas Müller at the University of Innsbruck in Austria explain why the changing colour of autumn leaves could be good news for your health

How green plant pigments disappear in the autumn, when the colours of the leaves of deciduous trees and shrubs change from green to red and yellow, has been a longstanding puzzle. While chlorophyll biosynthesis has been well studied, how chlorophyll breaks down remained a fascinating enigma until about 17 years ago. This lack of basic knowledge is all the more surprising, as chlorophyll metabolism is probably the most visible manifestation of life on Earth. In fact, it is even seen from outer space, and the total annual turnover of chlorophyll has been estimated to involve more than 1000 million tons.

In 1991 a colorless chlorophyll catabolite from senescent (aging) plant leaves was identified as a linear tetrapyrrole, which turned out to be distantly related to bilirubin and phytobilins, products of heme breakdown.[1] Since then, chlorophyll breakdown products have been identified in a variety of plant leaves, and their structural features revealed. According to these studies, chlorophyll breakdown in higher plants leads first to coloured compounds – as transient, enzyme-bound intermediates only. In a later stage, fluorescent catabolites occur merely fleetingly, and colourless, nonfluorescent tetrapyrrolic catabolites are formed rapidly. The latter accumulate in de-greening leaves and are considered the final products of chlorophyll breakdown, which apparently is a well controlled program for rapid detoxification of the photoactive green plant pigment.

But chlorophyll breakdown is not merely a detoxification process for the plant. It has also been associated with recycling of important nutrients, of reduced nitrogen, in particular. In the case of the catabolites, the four chlorophyll nitrogen atoms remain in the known tetrapyrrolic breakdown products and are thus not available for the plant to re-use. Nevertheless, they will eventually become part of more global recycling, possibly involving lower organisms.

Catabolites formed as fruit and leaves change colour may be valuable nutritional components

Recently, we addressed the puzzle of chlorophyll breakdown in ripening fruit. In freshly ripe apples and pears the very same linear tetrapyrroles were detected as chlorophyll catabolites. In fact, these breakdown products were also identical to the ones found in the de-greening leaves of the pear tree. Accordingly, chlorophyll breakdown appears to take a common pathway in fruit ripening and leaf senescence. As senescence is considered to accompany programmed cell death – yet ripening, commonly, is not – this finding is remarkable indeed.

In fruit, the tetrapyrrolic chlorophyll catabolites become a part of traditional food and may be a positive component in our diet as they are effective antioxidants. Exploratory studies have pointed to their beneficial health effects in mammals. Thus, the occurrence of such chlorophyll remains in apple peels may give a new twist to the old Welsh saying 'An apple a day, keeps the doctor away'.

140 years after Gregor Mendel used de-greening in peas as part of his experiments to establish the laws of inheritance, the basis for his observation is now known to be genetic control of chlorophyll breakdown. While the process may no longer be a total enigma, however, its wide-reaching benefits remain a field ripe for investigation.[2]

Read more in Bernhard Kräutler's perspective in Photochemical and Photobiological Sciences.

References

1 B Kräutler *et al*, *Angew. Chem., Int. Ed.*, 1991, **30**, 1315

2 B Kräutler, *Photochem. Photobiol. Sci.*, 2008, DOI: 10.1039/b802356p

Essential elements

Engineering success

CrystEngComm celebrated its tenth year of publication in style on 28 August with a lunch reception held at the XXI Congress and General Assembly of the International Union of Crystallography in Osaka, Japan. As part of the celebrations, the journal also awarded five poster prizes at the meeting.

Since its launch in 1999, *CrystEngComm* has gone from strength to strength, growing in size by more than a factor of ten. The journal now boasts the fastest publication times and highest immediacy index for a crystal engineering journal, plus an impressive impact factor of 3.47. In his welcome speech, *CrystEngComm* editor Jamie Humphrey outlined the successes of the past decade and extended his thanks: 'This success has been possible only through the support that you and other members of the crystal

engineering community have given the journal – your support as authors, referees, readers and in some cases editorial and advisory board members.'

Regular *CrystEngComm* author Pierangelo Metrangolo of Milan, Italy, who attended the lunch reception, cites the journal as one of his favourites for publication of his research. 'In particular,' he says, 'I appreciate the speed at which papers are processed and the very kind co-operation of the editorial staff. What else to say: Happy Birthday *CrystEngComm*..., and keep up the good work!'

A decade since launch and the future for *CrystEngComm* has never looked so bright. Celebrations will continue later this year with an anniversary theme issue, including articles by editorial and advisory board members, and the journal is also heavily involved in the organisation of a crystal engineering symposium as part of the IUPAC Congress next year in Glasgow.

Visit www.crystengcomm.org for updates on these and other exciting events.

Facebook fans

Enjoyed reading the first few issues of RSC Publishing's newest journal, *Energy & Environmental Science* (*EES*)? Then become a Facebook fan by visiting the *EES* Facebook page and joining in. Fans can see summaries and link to the latest *EES* articles published online, view and share relevant videos, images, events and news. Use the page to find out about upcoming events where you can meet the editors or contribute to a discussion and connect with fellow fans. Fans will see stories in their News Feed when their friends become fans or engage with the *EES* Facebook page in a variety of ways. You can find the *EES* Facebook page by searching for *Energy & Environmental Science* using the Quick Search bar on any Facebook page or by going to the main search page.

Or paste the following URL into your browser: www.facebook.com/pages/Energy-Environmental-Science/24375018213.

See you there!

A warm reception in Philadelphia

The atmosphere inside the Philadelphia Marriott mirrored the sunny blue sky outside as guests gathered at the RSC Reception. Held on 17 August, it coincided with the 236th American Chemical Society National Meeting and Exposition taking place at the Pennsylvania Convention Center.

Around 200 people listened to RSC president Dave Garner as he welcomed guests, including Nobel prize winner Bob Grubbs from Caltech,

Left to right: Jonathan Sessler (U Texas at Austin), Kate Sear (deputy editor ChemComm, RSC), Kevin Burgess (Texas A&M), Peter Wipf (Pittsburgh)

a variety of eminent and emerging researchers, plus university librarians and local RSC members. The incoming president of the ACS, Tom Lane, was also there with a number of his society colleagues, indicating the continuing warm friendship between the two chemical societies.

Guests enjoyed refreshments while catching up with friends old and new, and RSC staff were on hand to describe the latest RSC initiatives, including the hot topics of *Energy & Environmental Science*, *Integrative Biology* and *Metallomics*, the three newest RSC journals.

At the end of a genial evening, everyone was looking forward to meeting again – so see you all in Salt Lake City in spring 2009!

Chemical Biology (ISSN: 1747-1605) is published monthly by the Royal Society of Chemistry, Thomas Graham House, Science Park, Milton Road, Cambridge UK CB4 0WF. It is distributed free with *Chemical Communications*, *Organic & Biomolecular Chemistry*, *Molecular BioSystems*, *Natural Product Reports*, *Dalton Transactions* and *Photochemical & Photobiological Sciences*. *Chemical Biology* can also be purchased separately. 2008 annual subscription rate: £199; US $396. All orders accompanied by payment should be sent to Sales and Customer Services, RSC (address above). Tel +44 (0) 1223 432360, Fax +44 (0) 1223 426017. Email: sales@rsc.org

RSC Publishing