

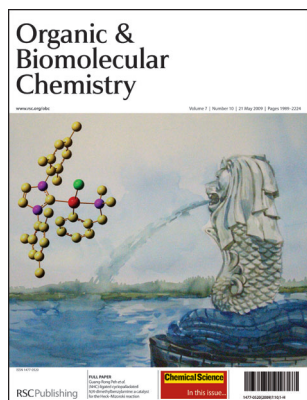
# Organic & Biomolecular Chemistry

An international journal of synthetic, physical and biomolecular organic chemistry  
[www.rsc.org/obc](http://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](http://www.rsc.org)

## IN THIS ISSUE

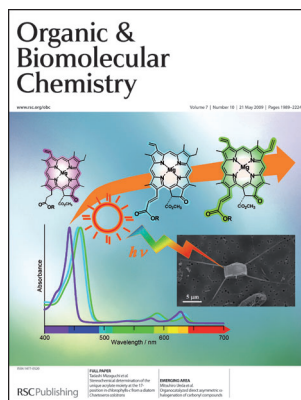
ISSN 1477-0520 CODEN OBCRAK 7(10) 1989–2224 (2009)



### Cover

See Guang-Rong Peh *et al.*, pp. 2110–2119.  
IMes-Pd(dmba)Cl is a highly active and practical Heck–Mizoroki precatalyst developed in Singapore, symbolized by the Merlion waterfront landmark. Artwork by Mr Sitthisak Saleeruang and Dr Eric Assen B. Kantchev.

Image reproduced by permission of Eric Assen B. Kantchev from *Organic & Biomolecular Chemistry*, 2009, **7**, 2110.



### Inside cover

See Tadashi Mizoguchi *et al.*, pp. 2120–2126.  
A diatom, *Chaetoseros calcitrans*, contains unique chlorophylls-c having a conjugated acrylate residue at the 17-position. The residue functions to expand the absorption region at around 400–500 nm for photosynthesis.

Image reproduced by permission of Hitoshi Tamiaki from *Organic & Biomolecular Chemistry*, 2009, **7**, 2120.

## CHEMICAL SCIENCE

### C33

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

May 2009/Volume 6/Issue 5

[www.rsc.org/chemicalscience](http://www.rsc.org/chemicalscience)

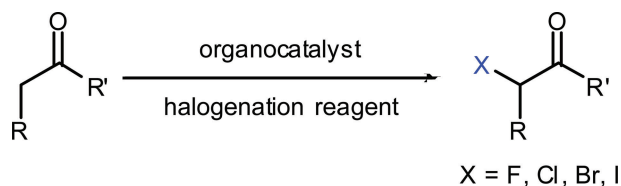
## EMERGING AREA

### 2005

#### Organocatalyzed direct asymmetric $\alpha$ -halogenation of carbonyl compounds

Mitsuhiro Ueda, Taichi Kano and Keiji Maruoka\*

The formation of carbon–halogen bonds in an enantioselective manner is an important reaction, because it leads to optically active halogen compounds, which are useful intermediates for further elaboration to other valuable compounds. This review article describes recent developments in asymmetric organocatalyzed halogenations.



## EDITORIAL STAFF

### Editor

Vikki Allen

### Deputy editor

Richard Kelly

### Assistant editor

Russell Johnson, Joanne Thomson

### Publishing assistant

Jess Doherty

### Assistant manager & Team leader, Informatics

Michelle Canning

### Technical editors

David Barden, Nicola Burton, Sandra Fanjul,  
Frances Galvin, Elinor Richards

### Administration coordinator

Sonya Spring

### Administration assistants

Aliya Anwar, Jane Orchard, Julie Thompson

### Publisher

Emma Wilson

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](mailto:sales@rscdistribution.org)

2009 Annual (print + electronic) subscription price: £2957; US\$5796. 2009 Annual (electronic) subscription price: £2661; US\$5216. 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](http://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](mailto:advertising@rsc.org)

For marketing opportunities relating to this journal, contact [marketing@rsc.org](mailto:marketing@rsc.org)

# Organic & Biomolecular Chemistry

An international journal of synthetic, physical and biomolecular organic chemistry

[www.rsc.org/obc](http://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.

## EDITORIAL BOARD

### Chair

Professor Jay Siegel, Zürich,  
Switzerland

Professor Jeffrey Bode, Philadelphia,  
USA

Professor Margaret Brimble,  
Auckland, New Zealand

Professor Ben Davis, Oxford, UK  
Dr Veronique Gouverneur, Oxford, UK  
Professor David Leigh, Edinburgh, UK  
Professor Mohamed Marahiel,  
Marburg, Germany  
Professor Stefan Matile, Geneva,  
Switzerland  
Professor Paolo Scrimin, Padova, Italy

Professor Brian Stoltz, Pasadena, USA  
Professor Keisuke Suzuki, Tokyo, Japan

## ADVISORY BOARD

Roger Alder, Bristol, UK  
Jeffrey Bode, Philadelphia, USA  
Helen Blackwell, Madison, USA  
John S Carey, Tonbridge, UK  
Barry Carpenter, Cardiff, UK  
Michael Crimmins, Chapel Hill, USA  
Antonio Echavarren, Tarragona,  
Spain  
Jonathan Ellman, Berkeley, USA  
Kurt Faber, Graz, Austria  
Ben Feringa, Groningen,  
The Netherlands  
Nobutaki Fujii, Kyoto, Japan  
Jan Kihlberg, Umea, Sweden  
Philip Kocienski, Leeds, UK

Steven V Ley, Cambridge, UK  
Zhang Li-He, Beijing, China  
Stephen Loeb, Ontario, Canada  
Ilan Marek, Haifa, Israel  
Manuel Martín Lomas,  
San Sebastián, Spain  
Keiji Maruoka, Kyoto, Japan  
Heather Maynard, Los Angeles,  
USA  
E W 'Bert' Meijer, Eindhoven,  
The Netherlands  
Eiichi Nakamura, Tokyo, Japan  
Ryoji Noyori, Nagoya, Japan  
Mark Rizzacasa, Melbourne,  
Australia

Oliver Seitz, Berlin, Germany  
Bruce Turnbull, Leeds, UK  
Chris Welch, Rahway, USA  
Peter Wipf, Pittsburg, USA  
Henry N C Wong, Hong Kong,  
China  
Sam Zard, Ecole Polytechnique,  
France

## 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>

Authors may reproduce/republish portions of their published contribution without seeking permission from the RSC, provided that any such republication is accompanied by an acknowledgement in the form: (Original citation) – Reproduced by permission of the Royal Society of Chemistry.

© The Royal Society of Chemistry, 2009. Apart from fair dealing for the purposes of research or private study for non-commercial purposes, or criticism or review, as permitted under the Copyright, Designs and Patents Act 1988 and the Copyright and Related Rights Regulations 2003, this publication may only be reproduced, stored or transmitted, in any form or by any means, with

the prior permission in writing of the Publishers or in the case of reprographic reproduction in accordance with the terms of licences issued by the Copyright Licensing Agency in the UK. US copyright law is applicable to users in the USA.

The Royal Society of Chemistry takes reasonable care in the preparation of this publication but does not accept liability for the consequences of any errors or omissions.

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

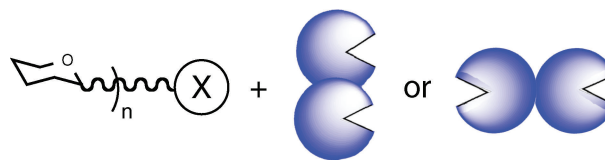
Royal Society of Chemistry: Registered Charity No. 207890

2013

**Maximising multivalency effects in protein–carbohydrate interactions**

Roland J. Pieters\*

Multivalency often improves the potency of carbohydrate ligands and inhibitors. In this perspective it is discussed how different target proteins need different multivalent ligand designs to maximise the multivalency effects.



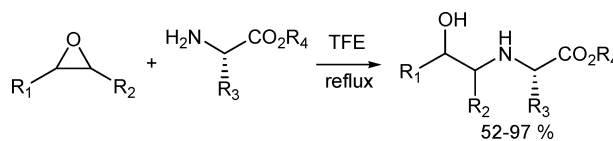
## COMMUNICATIONS

2026

**Non Lewis acid catalysed epoxide ring opening with amino acid esters**

Christine Philippe, Thierry Milcent, Benoit Crousse\* and Danièle Bonnet-Delpon

The ring opening of epoxides by various amino acid esters in refluxing trifluoroethanol without any catalyst is described. The corresponding  $\beta$ -amino alcohols are obtained in good to excellent yields.

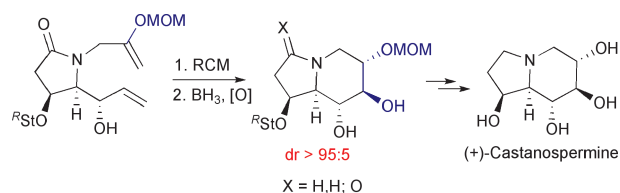


2029

**Asymmetric synthesis of (+)-castanospermine through enol ether metathesis–hydroboration/oxidation**

Julien Ceccon, Grégory Danoun, Andrew E. Greene and Jean-François Poisson\*

An asymmetric synthesis of (+)-castanospermine is presented in which enol ether metathesis–hydroboration/oxidation is used for stereoselective installation of the *trans-trans* hydroxyl groups on the piperidine ring of the alkaloid.

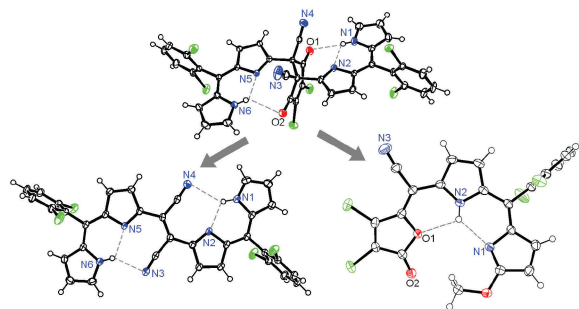


2032

**Facile synthesis of dicyanovinyl-di(*meso*-aryl)dipyrromethenes *via* a dipyrromethene–DDQ adduct**

Ji-Young Shin,\* Brian O. Patrick and David Dolphin\*

Dicyano-substituted vinyl dipyrromethene **4** (left) and compound **5** (right) were prepared from a simple *meso*-aryl dipyrromethane *via* the DDQ adduct **3**. The unique structures of **3**, **4** and **5** were confirmed by X-ray diffraction analysis.



ASMC  
KIEV 09

International Symposium on

# Advances in Synthetic and Medicinal Chemistry

August 23 - 27, 2009  
Kiev, Ukraine

Symposium Chairmen:

Dr. S. A. BILLER (NOVARTIS, Cambridge, United States)  
Prof. E. M. CARREIRA (ETH ZURICH, Zürich, Switzerland)

[www.asmc09.org](http://www.asmc09.org)

SYMPOSIUM SECRETARIAT: LD Organisation  
Tel : +32 10 45 47 77 - Fax : +32 10 45 97 19  
[secretariat@asmc09.org](mailto:secretariat@asmc09.org)

Organized by



CHEMBRIDGE CORPORATION



EFMC  
European Federation  
for Medicinal Chemistry

# No missing pieces

*Chemistry World* e-alerts are the perfect way to ensure you always see the complete picture.

Sign up now for free and keep up to date on all the latest chemistry news with a daily e-mail that lets you know what's new on the *Chemistry World* website.

**chemistryworld**  
e-alerts

RSC | Advancing the  
Chemical Sciences

[www.chemistryworld.org](http://www.chemistryworld.org)

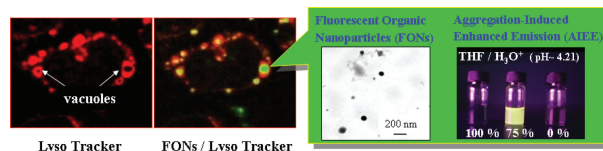
Registered Charity Number 207890

2036

### Fluorescent organic nanoparticle formation in lysosomes for cancer cell recognition

Hsin-Hung Lin, Sheng-Yuan Su and Cheng-Chung Chang\*

We developed a vacuole model using fluorescent organic nanoparticles to elucidate the formation of fluorescent bright spots in the lysosomes of cancer cells. It can be applied as a biomarker in cell biology.



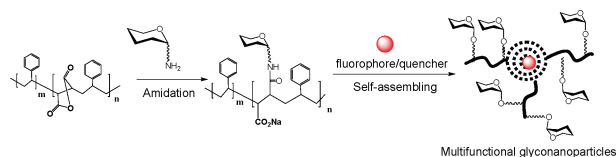
PAPERS

2040

### Multivalent mannose-displaying nanoparticles constructed from poly{styrene-co-[(maleic anhydride)-*alt*-styrene]}

Rongmin Su, Lei Li, Xiaoping Chen, Jiahuai Han and Shoufa Han\*

Multifunctional mannose-displaying nanoparticles, easily constructed from poly{styrene-co-[(maleic anhydride)-*alt*-styrene]}, bind selected lectins on cell surfaces with enhanced affinity while allowing direct spectrofluorimetric monitoring of lectin-glycan interactions.

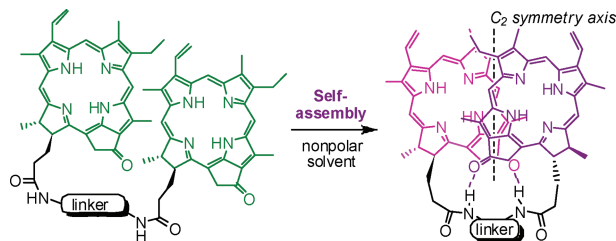


2046

### Hydrogen bond driven self-assembled $C_2$ -symmetric chlorin *syn* dimers; unorthodox models for chlorophyll 'special pairs' in photosynthetic reaction centres

Taru Nikkonen, Raisa Haavikko and Juho Helaja\*

In non-polar solvents amide bond linked chlorin dimers self-assemble into excitonically coupled, 'special pair' related,  $C_2$ -symmetric structures, by internal hydrogen bonding.

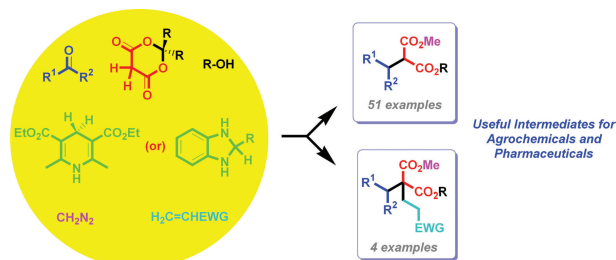


2053

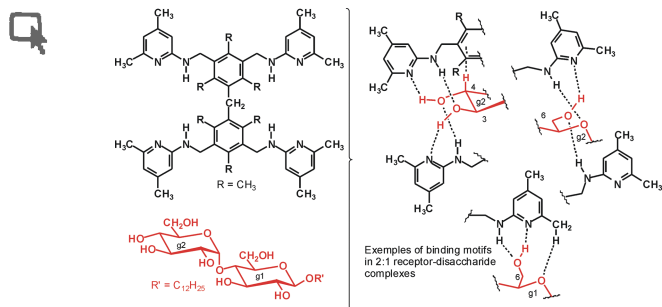
### Multi-catalysis cascade reactions based on the methoxycarbonylketene platform: diversity-oriented synthesis of functionalized non-symmetrical malonates for agrochemicals and pharmaceuticals

Dhevalapally B. Ramachary,\* Chintalapudi Venkaiah, Y. Vijayendar Reddy and Mamillapalli Kishor

An economic, environmentally friendly, one-pot, multi-catalysis cascade synthesis of non-symmetrical malonates has been developed. Many of the products have direct application in agrochemical and pharmaceuticals.



2063

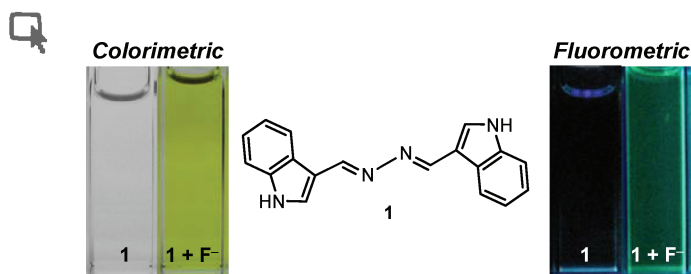


### Recognition properties of receptors based on dimesitylmethane-derived core: Di- vs. monosaccharide preference

Monika Mazik\* and Arno C. Buthe

Dimesitylmethane-based receptors, incorporating four heterocyclic recognition units capable of serving as hydrogen bonding sites, show high binding affinity toward  $\alpha$ - and  $\beta$ -maltoside, as well as a strong di- vs. monosaccharide preference.

2072

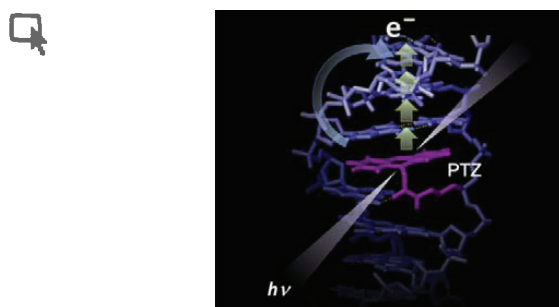


### Indole-azadiene conjugate as a colorimetric and fluorometric probe for selective fluoride ion sensing

Yasuhiro Shiraishi,\* Hajime Maehara and Takayuki Hirai

An indole-azadiene conjugate (**1**), synthesized by facile one-step condensation, behaves as a highly selective probe for fluoride ion both in colorimetric and fluorometric analyses.

2077

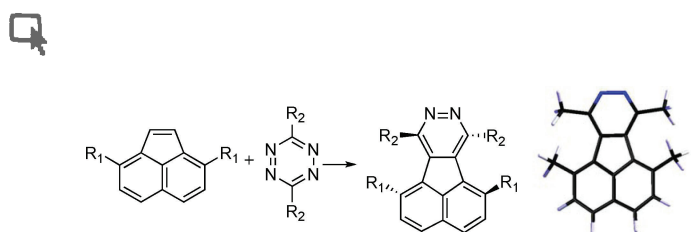


### Pathways of excess electron transfer in phenothiazine-tethered DNA containing single-base mismatches

Takeo Ito,\* Akiko Kondo, Tomoyuki Kamashita, Kazuhito Tanabe, Hisatsugu Yamada and Sei-ichi Nishimoto\*

Photo-induced electron injection from phenothiazine (PTZ) and the succeeding electron transfer in DNA containing single-base mismatches was studied to understand the effects of local structural changes on DNA-mediated excess electron transfer reaction.

2082



### Diels–Alder reactions of 3,6-disubstituted 1,2,4,5-tetrazines. Synthesis and X-ray crystal structures of diazafluoranthene derivatives

Nelli Rahanyan, Anthony Linden, Kim K. Baldridge and Jay S. Siegel\*

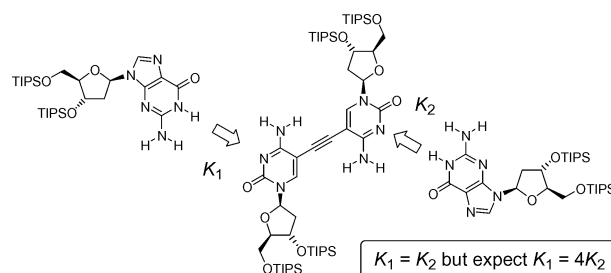
Inverse-demand Diels–Alder chemistry leads to a class of structurally characterized twisted diazafluoranthenes, potential precursors to bowl-shaped heterocycles.

2093

### Apparent non-statistical binding in a ditopic receptor for guanosine

Asawin Likhitsup, Robert J. Deeth, Sijbren Otto and Andrew Marsh\*

We observe non-statistical binding for guanosine associating with a ditopic cytidine-bearing receptor built around one alkyne, but not for guanosine interacting with a longer, homologous dialkyne.

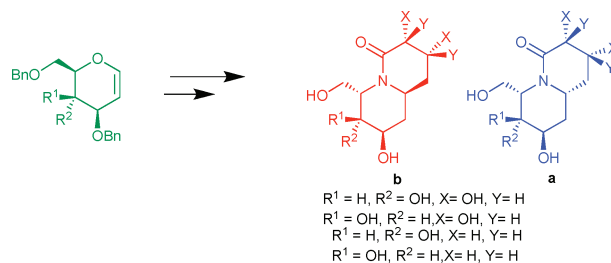


2104

### Synthesis and glycosidase-inhibitory activity of novel polyhydroxylated quinolizidines derived from D-glycals

Nitee Kumari and Yashwant D. Vankar\*

Novel polyhydroxylated quinolizidines have been prepared starting from D-glycals following a methodology developed in our laboratory for chloroamidation of olefins. All synthesized final molecules were found to be selective against certain glycosidases.

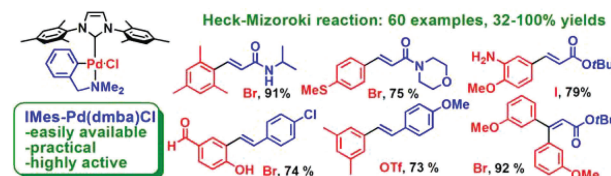


2110

### N-heterocycle carbene (NHC)-ligated cyclopalladated N,N-dimethylbenzylamine: a highly active, practical and versatile catalyst for the Heck–Mizoroki reaction

Guang-Rong Peh, Eric Assen B. Kantchev,\* Chi Zhang and Jackie Y. Ying\*

An easily prepared, air- and moisture-stable, well-defined NHC-palladacycle mediates the single and double Heck–Mizoroki reaction of a number of functionalized aryl bromides, iodides and triflates with acrylic esters, amides and styrene derivatives in good to excellent yields.

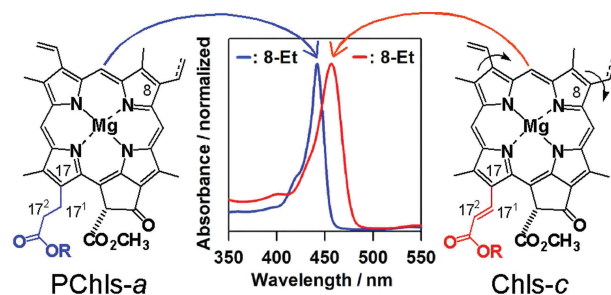


2120

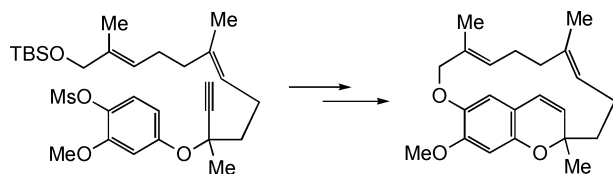
### Stereochemical determination of the unique acrylate moiety at the 17-position in chlorophylls-c from a diatom *Chaetoseros calcitrans* and its effect upon electronic absorption properties

Tadashi Mizoguchi, Chihiro Nagai, Michio Kunieda, Yuki Kimura, Atsushi Okamura and Hitoshi Tamiaki\*

The 17-acrylate in chlorophylls (Chls)-c took the *cisoid* rotamer exclusively, and Chls-c had red-shifted and broadened Soret bands in comparison with the corresponding 17<sup>1</sup>,17<sup>2</sup>-dihydrogenated PChls-a.



2127

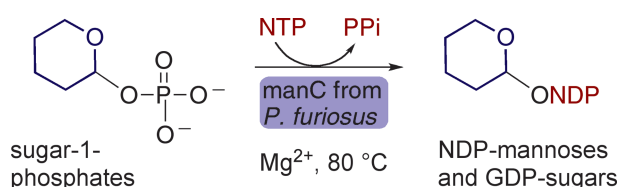


### Synthesis of (±)-likonide B (smenochromene D) using a regioselective Claisen rearrangement, separation of the enantiomers and stereochemical assignment

Marjorie Bruder, Stephen J. Smith, Alexander J. Blake and Christopher J. Moody\*

A synthesis of the ansa-bridged farnesyl hydroquinone (±)-likonide B is described, in which the key steps are a regioselective microwave-mediated Claisen rearrangement of an aryl propargyl ether and macrocyclization *via* an intramolecular Mitsunobu reaction.

2135

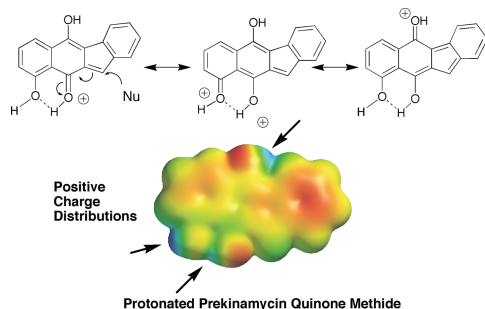


### Phosphomannose isomerase/GDP-mannose pyrophosphorylase from *Pyrococcus furiosus*: a thermostable biocatalyst for the synthesis of guanidinediphosphate-activated and mannose-containing sugar nucleotides

Rahman M. Mizanur and Nicola L. B. Pohl\*

A recombinant hyperthermostable, bifunctional enzyme proves amenable to one-pot syntheses of a range of GDP-activated sugars and NDP-mannoses.

2140

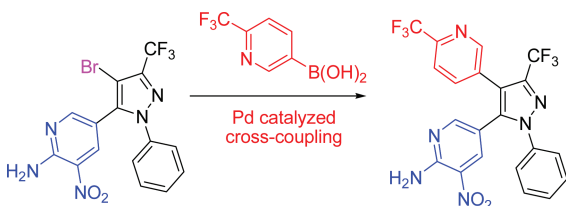


### Quinone methide chemistry of prekinamycins: <sup>13</sup>C-labeling, spectral global fitting and in vitro studies

Omar Khmour and Edward B. Skibo\*

Calculations of electron densities for the prekinamycin quinone methide and its protonated form suggest that cation formation by protonation may be required for nucleophilic trapping by the 5-centre.

2155



### Trifluoromethyl-substituted pyridyl- and pyrazolylboronic acids and esters: synthesis and Suzuki–Miyaura cross-coupling reactions

Kate M. Clapham, Andrei S. Batsanov, Martin R. Bryce\* and Brian Tarbit

Highly-functionalised pyridine and pyrazole derivatives incorporating trifluoromethyl substituents have been synthesised by Suzuki–Miyaura cross-coupling protocols.

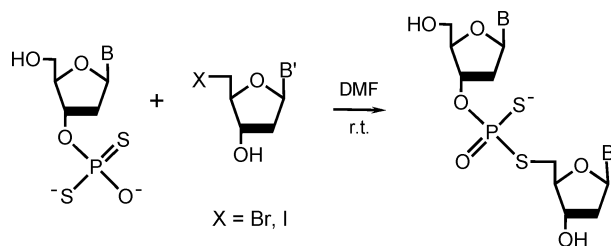


2162

**The synthesis of di- and oligo-nucleotides containing a phosphorodithioate internucleotide linkage with one of the sulfur atoms in a 5'-bridging position**

Magdalena Olesiak, Wojciech J. Stec and Andrzej Okruszek\*

A new type of internucleotide phosphorodithioate linkage is described, wherein one of the sulfur atoms occupies a 5'-bridging position. Representative dinucleotides (or corresponding dinucleotide building blocks) were synthesized by *S*-alkylation of nucleoside-3'-*O*-phosphorodithioates with 5'-halogeno-5'-deoxy-nucleosides.

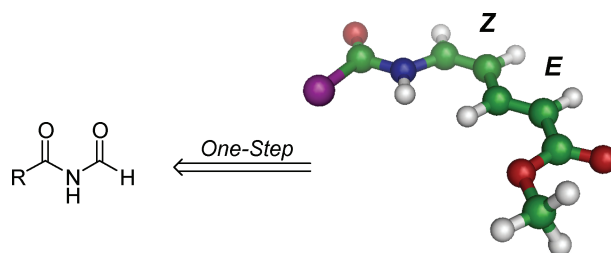


2170

**Fast and efficient one step synthesis of dienamides**

Jennifer E. Mathieson, James J. Crawford, Marc Schmidtman and Rodolfo Marquez\*

A fast and efficient one-step approach to the synthesis of dienamides is reported. This concise methodology relies on the use of imides as reactive intermediates and allows for the preferential formation of *Z,E*-dienamides in good yields.

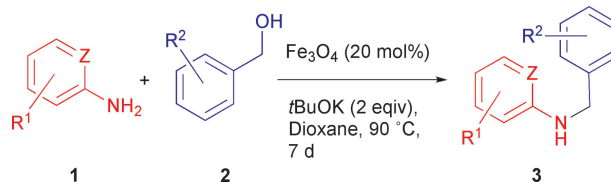


2176

**Selective *N*-monoalkylation of aromatic amines with benzylic alcohols by a hydrogen autotransfer process catalyzed by unmodified magnetite**

Ricardo Martínez, Diego J. Ramón\* and Miguel Yus\*

Magnetite is a good catalyst for the selective *N*-alkylation of aromatic amines under mild conditions, with the catalyst easily being recycled eight times by a simple magnet without losing activity.

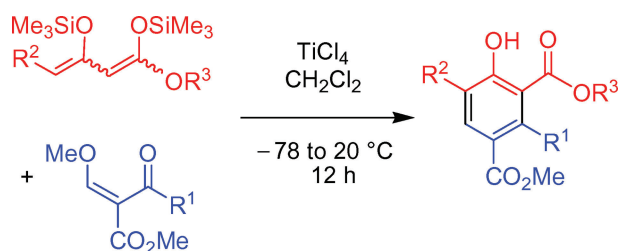


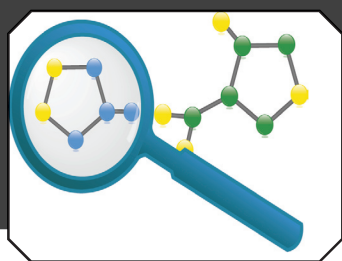
2182

**Diversity-oriented synthesis of 1-hydroxy-2,4-benzodioxates by regioselective [3+3] cyclocondensations of 1,3-bis(silyloxy)-1,3-butadienes with 3-alkoxy- and 3-silyloxy-2-alkoxycarbonyl-2-en-1-ones**

M. Shkoor, A. Riahi, O. Fatunsin, I. Hussain, M. A. Yawer, M. Lubbe, S. Reim, H. Reinke, C. Fischer and P. Langer\*

A variety of functionalized 1,3-benzodioxates were regioselectively prepared by the first [3+3] cyclocondensations of 1,3-bis(silyloxy)-1,3-butadienes with 3-alkoxy- and 3-silyloxy-2-alkoxycarbonyl-2-en-1-ones.





# FRAGMENT - BASED LEAD DISCOVERY SUMMIT

26 June 2009 London, England

Select Biosciences' inaugural Fragment-Based Lead Discovery Summit will be a one day symposium designed to present the latest advances within the field.

This meeting will be one of several one day events that will focus on the drug discovery sector.

## Confirmed Speakers:

**Sir Tom Blundell**, Professor and Research Head,  
University of Cambridge

**Daniela Fattori**, Chemistry Department Head,  
Menarini Ricerche

**Rod Hubbard**, Lab Head, University of York

**Renate Sekul**, CSO, Graffinity

**Helena Danielson**, Professor, Uppsala University

**Richard B. Silverman**, Professor, Northwestern  
University

**Gregg Siegal**, Professor, Leiden University

**Gordon Saxty**, Medicinal Chemist, Astex  
Therapeutics

**Maurizio Pellecchia**, Professor, Burnham Institute  
for Medical Research

For sponsorship and exhibition opportunities contact Aaron Woodley  
tel: +44 (0) 1787 315129 email: a.woodley@selectbiosciences.com



## Agenda Topics

- Fragment-Based Lead Discovery
- Biophysical Methods for Maintaining Fragment Binding
- NMR Based Fragment Screening Technologies
- The Suitability of SPR Based Fragment Screening

[FBLDSUMMIT.COM](http://FBLDSUMMIT.COM)

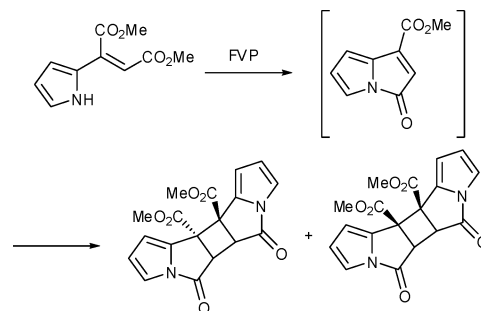
**SELECT  
BIOSCIENCES**  
*Delivering the Difference*

2187

### 1-Methoxycarbonylpyrrolizin-3-one and related compounds

Xavier L. M. Despinoy and Hamish McNab\*

Flash vacuum pyrolysis (FVP) of dimethyl *E*- or *Z*-pyrrol-2-ylbut-2-enedioate at 700 °C gives 1-methoxycarbonylpyrrolizin-3-one. The sequence involves elimination of methanol and cyclisation; the elimination step is rate determining. The pyrrolizinone dimerises spontaneously at room temperature across the 1,2-bond to give a mixture of *trans*- and *cis*-7,8-dioxo-7,7a,7b,8-tetrahydro-6a,8a-diazacyclobuta[1,2-*a*;4,3-*a'*]dipentalene-3b,3c dicarboxylates.

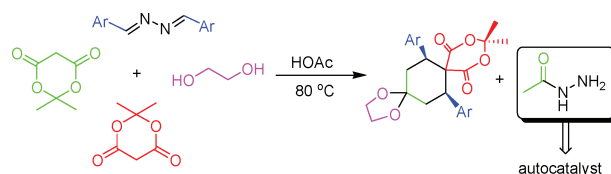


2195

### A new domino autocatalytic reaction leading to polyfunctionalized spiro[5.5]undecanes and dispiro[4.2.5.2]pentadecanes

Bo Jiang, Wen-Juan Hao, Jin-Peng Zhang, Shu-Jiang Tu\* and Feng Shi

A new domino autocatalytic reaction of imines with Meldrum's acid to polycyclic spiro[5.5]undecane-1,5,9-trione and dispiro[4.2.5.2]-pentadecane-9,13-dione derivative with remarkable diastereoselectivity was described. In this reaction, up to six new bonds were formed accompanied by the C=N bond cleavage of the imines.

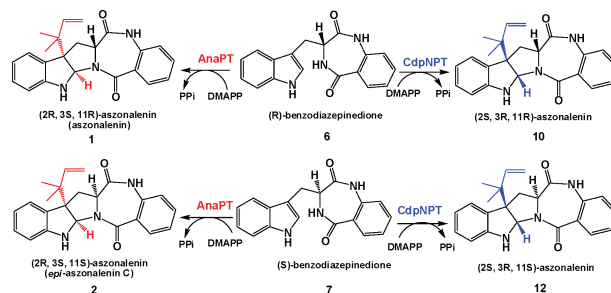


2202

### Stereospecific synthesis of aszonalenins by using two recombinant prenyltransferases

Wen-Bing Yin, Jun Cheng and Shu-Ming Li\*

Both AnaPT and CdpNPT catalysed the C3-prenylation of (*R*)- and (*S*)-benzodiazepinedione, but introduced the prenyl moieties from opposite sides of the indoline ring. By using these enzymes, four aszonalenin stereoisomers were synthesized with a stereoselectivity of nearly 100% and conversion rates of 85–100% in one-step reactions.

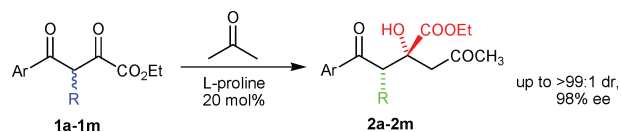


2208

### Highly diastereo- and enantioselective organocatalytic addition of acetone to $\beta$ -substituted $\alpha$ -ketoesters via dynamic kinetic resolution

Jin Yang, Ting Wang, Zhenhua Ding, Zongxuan Shen and Yawen Zhang\*

L-Proline catalyzes the aldol addition reaction of acetone to  $\beta$ -substituted  $\alpha$ -ketoesters with dynamic kinetic resolution, providing the adduct in good yield with excellent diastereo- and enantioselectivity. A tentative explanation for the stereochemical outcome is given.

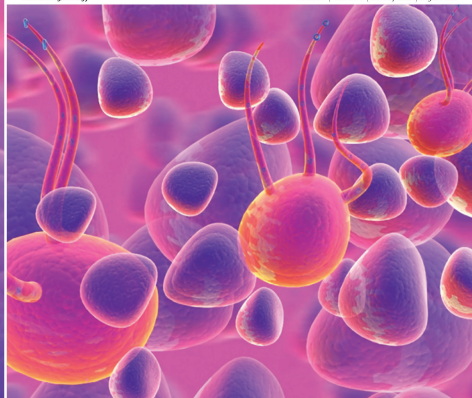


# Integrative Biology

Quantitative biosciences from nano to macro

www.rsc.org/ibiology

Volume 1 | Number 1 | January 2009 | Pages 1-100



ISSN 1751-0754

RSC Publishing



1751-0754(2009)1:1;1-100

New for  
2009

## Mary Helen Barcellos-Hoff, Scientific Editor, *Integrative Biology*

Mary Helen Barcellos-Hoff is a Professor in the department of Radiation Oncology at the New York University Langone School of Medicine. As an undergraduate at the University of Chicago, she conducted neuroanatomy studies using electron microscopy. Mary Helen obtained her doctorate in Experimental Pathology at the University of California, San Francisco, for studies in cell interactions during brain cancer therapy, and postgraduate research at University of California, Berkeley on functional analysis of mammary lactation. With collaborators at Lawrence Berkeley National Laboratory she developed imaging bioinformatic tools for high throughput microscopy. The goal is a systems biology analysis of radiation effects and consequences that integrates image information and functional data. Her current research program at New York University focuses on how ionizing radiation alters multicellular interactions during cancer development.

### Submit your work to *Integrative Biology*

Professor Barcellos-Hoff will be delighted to receive submissions from North America for *Integrative Biology*. Submissions are welcomed via ReSource, our homepage for authors and referees at [www.rsc.org/resource](http://www.rsc.org/resource)



"We believe that the integration of technology and quantitation will drive future biological paradigms."

RSC Publishing

[www.rsc.org/ibiology](http://www.rsc.org/ibiology)

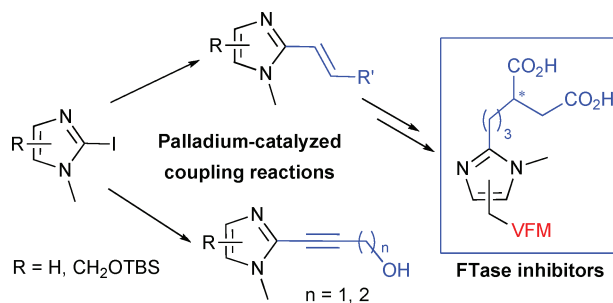
Registered Charity Number 207890

2214

## New asymmetric synthesis of protein farnesyltransferase inhibitors *via* palladium-catalyzed cross-coupling reactions of 2-iodo-imidazoles

Jennifer Kerhervé, Candice Botuha and Joëlle Dubois\*

The Suzuki methodology was found to be the most effective palladium catalyzed cross-coupling reaction to synthesize in few steps enantiomerically pure 2-propylsuccinyl imidazole derivatives from chiral alkenyl boronate esters.



## AUTHOR INDEX

Baldrige, Kim K., 2082  
 Batsanov, Andrei S., 2155  
 Blake, Alexander J., 2127  
 Bonnet-Delpon, Danièle, 2026  
 Botuha, Candice, 2214  
 Bruder, Marjorie, 2127  
 Bryce, Martin R., 2155  
 Buthe, Arno C., 2063  
 Cecon, Julien, 2029  
 Chang, Cheng-Chung, 2036  
 Chen, Xiaoping, 2040  
 Cheng, Jun, 2202  
 Clapham, Kate M., 2155  
 Crawford, James J., 2170  
 Crousse, Benoit, 2026  
 Danoun, Grégory, 2029  
 Death, Robert J., 2093  
 Despinoy, Xavier L. M., 2187  
 Ding, Zhenhua, 2208  
 Dolphin, David, 2032  
 Dubois, Joëlle, 2214  
 Fatunsin, O., 2182  
 Fischer, C., 2182  
 Greene, Andrew E., 2029  
 Haavikko, Raisa, 2046  
 Han, Jiahuai, 2040  
 Han, Shoufa, 2040  
 Hao, Wen-Juan, 2195


Helaja, Juho, 2046  
 Hirai, Takayuki, 2072  
 Hussain, I., 2182  
 Ito, Takeo, 2077  
 Jiang, Bo, 2195  
 Kamashita, Tomoyuki, 2077  
 Kano, Taichi, 2005  
 Kantchev, Eric Assen B., 2110  
 Kerhervé, Jennifer, 2214  
 Khdour, Omar, 2140  
 Kimura, Yuki, 2120  
 Kishor, Mamillapalli, 2053  
 Kondo, Akiko, 2077  
 Kumari, Nitee, 2104  
 Kunieda, Michio, 2120  
 Langer, P., 2182  
 Li, Lei, 2040  
 Li, Shu-Ming, 2202  
 Likhitsup, Asawin, 2093  
 Lin, Hsin-Hung, 2036  
 Linden, Anthony, 2082  
 Lubbe, M., 2182  
 Maehara, Hajime, 2072  
 Marquez, Rodolfo, 2170  
 Marsh, Andrew, 2093  
 Martínez, Ricardo, 2176  
 Maruoka, Keiji, 2005  
 Mathieson, Jennifer E., 2170

Mazik, Monika, 2063  
 McNab, Hamish, 2187  
 Milcent, Thierry, 2026  
 Mizanur, Rahman M., 2135  
 Mizoguchi, Tadashi, 2120  
 Moody, Christopher J., 2127  
 Nagai, Chihiro, 2120  
 Nikkonen, Taru, 2046  
 Nishimoto, Sei-ichi, 2077  
 Okamura, Atsushi, 2120  
 Okruszek, Andrzej, 2162  
 Olesiak, Magdalena, 2162  
 Otto, Sijbren, 2093  
 Patrick, Brian O., 2032  
 Peh, Guang-Rong, 2110  
 Philippe, Christine, 2026  
 Pieters, Roland J., 2013  
 Pohl, Nicola L. B., 2135  
 Poisson, Jean-François, 2029  
 Rahanyan, Nelli, 2082  
 Ramón, Diego J., 2176  
 Ramachary, Dhevalapally B., 2053  
 Reddy, Y. Vijayendar, 2053  
 Reim, S., 2182  
 Reinke, H., 2182  
 Riahi, A., 2182  
 Schmidtman, Marc, 2170  
 Shen, Zongxuan, 2208

Shi, Feng, 2195  
 Shin, Ji-Young, 2032  
 Shiraiishi, Yasuhiro, 2072  
 Shkoor, M., 2182  
 Siegel, Jay S., 2082  
 Skibo, Edward B., 2140  
 Smith, Stephen J., 2127  
 Stec, Wojciech J., 2162  
 Su, Rongmin, 2040  
 Su, Sheng-Yuan, 2036  
 Tamiaki, Hitoshi, 2120  
 Tanabe, Kazuhito, 2077  
 Tarbit, Brian, 2155  
 Tu, Shu-Jiang, 2195  
 Ueda, Mitsuhiro, 2005  
 Vankar, Yashwant D., 2104  
 Venkaiah, Chintalapudi, 2053  
 Wang, Ting, 2208  
 Yamada, Hisatsugu, 2077  
 Yang, Jin, 2208  
 Yawer, M. A., 2182  
 Yin, Wen-Bing, 2202  
 Ying, Jackie Y., 2110  
 Yus, Miguel, 2176  
 Zhang, Chi, 2110  
 Zhang, Jin-Peng, 2195  
 Zhang, Yawen, 2208

## FREE E-MAIL ALERTS AND RSS FEEDS


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

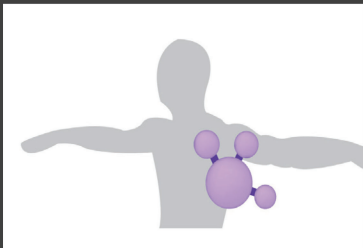
 Try our RSS feeds for up-to-the-minute news of the latest research. By setting up RSS feeds, preferably using feed reader software, you can be alerted to the latest Advance Articles published on the RSC web site. Visit [www.rsc.org/publishing/technology/rss.asp](http://www.rsc.org/publishing/technology/rss.asp)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



# MOLECULAR DIAGNOSTICS WORLD CONGRESS

6-7 August 2009 South San Francisco, CA, USA

Welcome to the 2nd Molecular Diagnostics World Congress

The conference will be co-located with the Microarray World Congress and Lab-on-a-Chip World Congress. Registered delegates will also have access to these meetings ensuring a very cost-effective trip.

### The distinguished faculty includes:

**Samir Hanash**, Program Head, Molecular Diagnostics, Fred Hutchinson Cancer Research Center

**John Quackenbush**, Professor, Harvard School of Public Health

**Edward Abrahams**, Executive Director, Personalised Medicine Coalition

**Johan Skog**, Instructor at Harvard Medical School, Assistant at Massachusetts General Hospital Neurology Unit

**Yi-Wei Tang**, Associate Professor, Vanderbilt University Medical Centre

**Huimin Kong**, Chief Scientific Officer, BioHelix Corporation

**Rona DeMarco**, Nanostrings Technologies

**Mike G. Makrigiorgos**, Associate Professor, Dana Farber Cancer Institute

**Emmanuel Monnet**, Head of Biomarkers Merck Serono

**Danxin Wang**, Research Scientist, The Ohio State University

**Yaron Kinar**, Research Scientist, Compugen

**Bruce Schiamber**, Research Analyst, Lux Research

**Norman C. Nelson**, Director of BioChemistry, Gen-Probe

**Galina Fomovska**, Senior Principal Scientist, Pall Life Sciences

**Vladimir Tolstikoc**, Director, Core Facility, University College Davis

**Walter Gall**, Programme Manager, Diagnostics Development, Metabolon

**Enal Razvi**, Biotechnology Analyst, Select Biosciences

### Be part of the event

We are currently accepting poster submissions. Deadlines and further details can be found online.

For sponsorship and exhibition opportunities contact Aaron Woodley  
**tel:** +44 (0) 1787 315129 **email:** a.woodley@selectbiosciences.com



### Agenda Topics

- Molecular Diagnostics & Biomarkers
- PGx and Personalized Medicine
- Emerging Technologies
- Clinical Applications of Molecular Diagnostics
- Commercial & Regulatory Perspectives

MOLECULARDIAGNOSTICS  
CONGRESS.COM

**SELECT  
BIOSCIENCES**  
*Delivering the Difference*

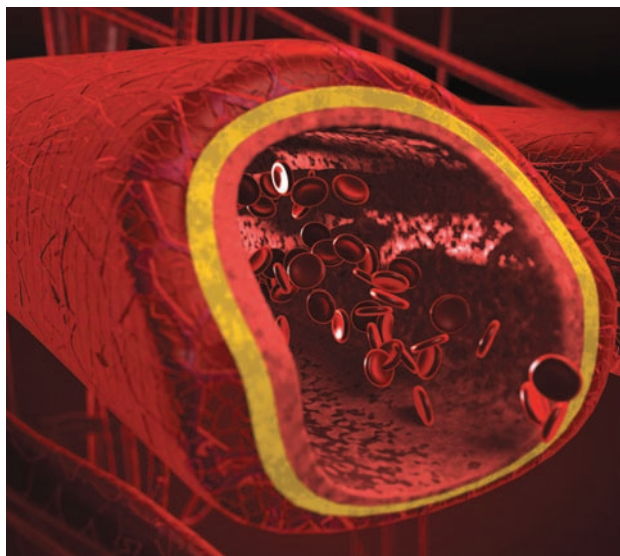
# Chemical Science

## Korean scientists have found an effective way of making biocompatible implants Polymers keep the blood flowing

Drug-laden polymer coats could make medical implants more biocompatible, according to scientists in Korea.

Dong Lyun Cho and colleagues at Chonnam National University in Gwangju have developed a method of coating stents in polymer and then attaching drug molecules to the surface. Stents are narrow mesh-like metal tubes that can be inserted into the diseased parts of arteries and then expanded to hold them open and keep the blood flowing. However, being foreign objects, stents can cause abnormal cell growth and artery narrowing (restenosis). The stents can be coated with polymers to avoid this. However, for a successful result, the polymer needs to be both biocompatible and strongly fixed to the metal surface, which Cho says is difficult to achieve.

Starting from a diamine monomer, Cho's team created a strongly adhesive polymer film on the stent's surface using a two-stage plasma polymerisation process. This method uses a high-



energy plasma to generate the reactive species needed to get the polymerisation started, and is an excellent way of producing thin pinhole-free films, says Cho. They then used the amino groups on the polymer surface to form amide bonds with  $\alpha$ -lipoic acid, a drug

**The implants hold diseased arteries open and deliver drugs**

**Reference**  
S-J Song *et al*, *J. Mater. Chem.*, 2009, DOI: 10.1039/b813357c

known to inhibit abnormal cell growth.

The new polymer films have high mechanical stability, says Cho, and prevent platelet aggregation in vitro. In addition, when tested on a model cell system, the new stents result in lower restenosis rates. Cho says that the key to these benefits is the  $\alpha$ -lipoic acid, since stents coated with a different anticoagulant, heparin, were not as successful at reducing restenosis. Future work, he adds, will involve investigating the long-term clinical effect of their stents.

Ketul Popat from the department of mechanical engineering at Colorado State University, Colorado, US, says that biocompatible surfaces that can prevent inflammation are critical for successful implants. Techniques such as those developed by Cho's team, he suggests, 'will be beneficial in overcoming several of the challenges that current stent technology faces.'  
*David Barden*

## In this issue

### Waste not, want not

Bacteria offer an easier way to convert biodiesel waste into useful chemicals

### A little more sensitivity

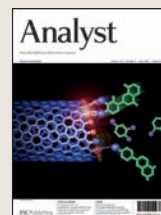
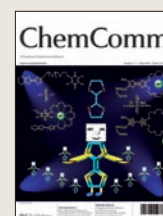
Fluorescent sensors to detect pH changes in a biological cell

### Living longer, disease-free

This month's Instant insight discusses our need for better methods to detect age-related diseases

### Making logical connections

Henry Rzepa talks about the potential for creativity in both research and teaching activities



A snapshot of the latest developments from across the chemical sciences

# Research highlights

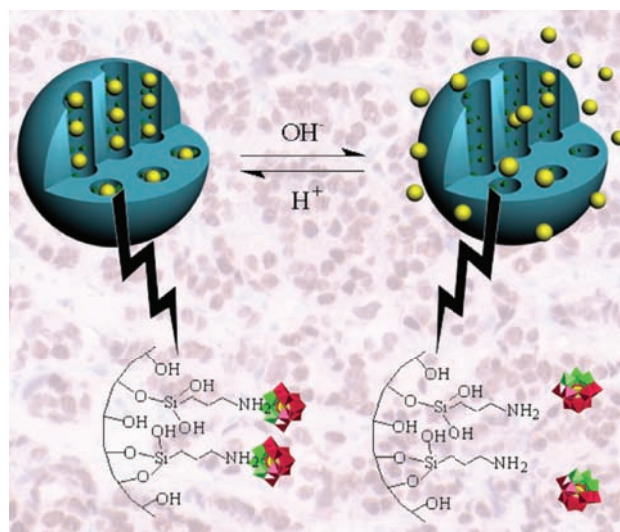
Colon cancer drug could reach its target without being destroyed by stomach acid

## Back to basics for drug delivery

Chinese chemists have developed a pH-responsive system that could deliver anticancer drugs to the colon without being broken down by stomach acid.

Enbo Wang from Northeast Normal University, Changchun, China, and colleagues attached a polyoxometalate (POM), through a dative bond, to mesoporous silica spheres. POMs are metal–oxygen cluster compounds that show a wide range of antiviral and anticancer activities. Though they are typically easier and cheaper to synthesise than their small-molecule organic pharmaceutical counterparts, scientists have found it difficult to stabilise and selectively deliver them to their intended therapeutic targets.

Wang tested his silica-bound POM's stability under acidic, basic and neutral conditions, replicating the conditions that they would come across travelling through the human digestive system to get to their target.



He found that the loading and release of the POM from the silica spheres is controlled by the pH value of the surrounding environment. A base triggers the dative bond to break,

**Drug release is caused by bonds breaking under basic conditions in the colon**

releasing the POM. Acidic conditions, such as those found in the stomach, and neutral conditions don't affect the bond, meaning that the POM will only be released once it has reached the basic conditions in the colon. The team also tested the POM's activity against cancer cells in vitro and found that incorporating the POM into silica spheres actually increased its activity.

'The pH-responsive controlled-release principle is likely to be of benefit for a variety of transition metal-containing drugs,' says Wang. Eric Maatta, an expert in transition metal systems from Kansas State University, Manhattan, US, agrees. He says that 'the strategy will likely be applicable to the delivery of other classes of anti-tumour agents and enhances the prospects for POM-based therapies'. *David Parker*

### Reference

G Sun *et al*, *Dalton Trans.*, 2009, DOI: 10.1039/b901133a

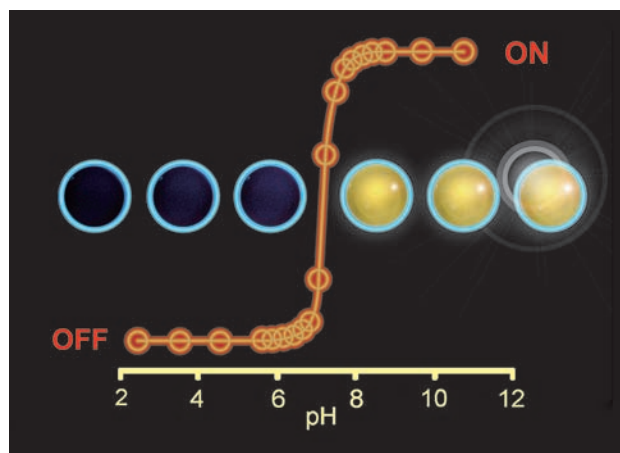
Scientists develop fluorescent sensors to detect pH changes in a biological cell

## A little more sensitivity

Fluorescent pH sensors that are so sensitive they can detect changes within almost a pH unit have been developed by Japanese researchers. The digital sensors could be used in molecular computers and to monitor pH changes in biological cells, say the scientists.

Seiichi Uchiyama and Yumi Makino at the University of Tokyo made the sensors by incorporating water-sensitive fluorophores into pH-responsive polymers. The polymers' structures vary with pH, from a hydrated open form at low pH to a dehydrated globular form at high pH. The sharp fluorescence signals given at each stage within a pH unit make them effective digital sensors. Different polymer structures can cover different pH ranges.

Dongwhan Lee, an expert in molecular sensors from Indiana University, Bloomington, US, says that it is the polymers' innovative design that allows them to give such



a sharp fluorescent response to pH change.

'Our sensors can be used to detect a subtle change in intracellular pH,' says Uchiyama. Conventional sensors are sensitive to an 80-fold change in pH whereas Uchiyama's sensors require only a five-fold

**The sensors can detect changes within a pH unit**

change. As well as changing the operating pH range, modifying the proton-recognising groups on the polymers can also tune the switching direction (on-off and off-on actions).

Uchiyama says that in the future, he hopes to incorporate different ion sensors into the structures to detect biological ions other than protons.

He adds: 'Molecular computing is the most exciting and challenging application for fluorescent digital ion sensors. There are many scientific papers about molecular logic and computing that use conventional fluorescent sensors. Our highly efficient devices could easily be combined with this concept to further develop molecular computing.'

*Harriet Brewerton*

### Reference

S Uchiyama and Y Makino, *Chem. Commun.*, 2009, DOI: 10.1039/b900889f



## Bacteria offer an easier way to convert biodiesel waste into useful chemicals

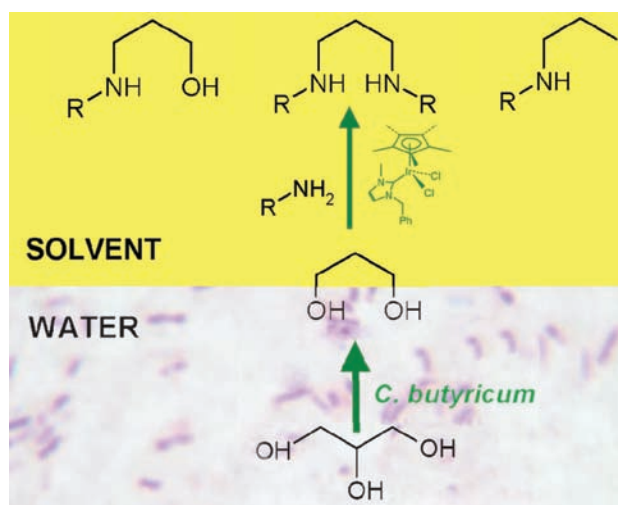
# Waste not, want not

UK scientists have converted crude biodiesel waste into useful amines with no need for difficult separation techniques.

Glycerol is produced in significant quantities as a by-product in biodiesel production, making it a cheap renewable feedstock for the chemical industry. For example, using microbial processes to ferment glycerol is an attractive route to 1,3-propanediol, which can be used as a precursor to high value polymers and platform chemicals. However, the fermentation products are produced in dilute solutions along with cell material and other metabolic products, making purification and separation difficult.

Now a team of scientists, led by Andrew Marr at Queen's University Belfast and Gillian Stephens at the University of Manchester, has combined microbial and transition metal catalysed processes to produce secondary amines without having to isolate and purify the diol intermediate.

Marr and Stephens treated glycerol



**Glycerol waste was treated with *C. butyricum* to produce secondary amines**

**Reference**  
S Liu *et al.*, *Chem. Commun.*, 2009, DOI: 10.1039/b820657k

with the bacterium *Clostridium butyricum*, then centrifuged the mixture of bacteria, 1,3-propanediol and by-products to remove the cells. The team then added a solution of an iridium catalyst, base and aniline in toluene to the solution, creating a biphasic mixture. After 24 hours at 115°C, 20 per cent of the 1,3-

propanediol had been converted to secondary amine.

'As fossil fuels become less accessible, chemists need to start developing new methods to convert renewable feedstocks into the chemical products and materials that society demands,' says Marr. 'Our key advance is to integrate biocatalytic and chemocatalytic processes to avoid the need to separate the fermentation products.'

'This is an important example of adding value to renewable resources,' says Mark Harmer, a research fellow at DuPont, Delaware, US. 'The ability to use all of the components from renewable feedstocks will be key to developing a biorefinery to replace the current oil-based refinery.'

Stephens agrees: 'The new approach will allow a myriad of chemical products to be derived from a single fermentation mixture. The microbiology can also be changed, allowing conversion of a wide range of feedstocks to diverse fermentation products.'

Vikki Chapman

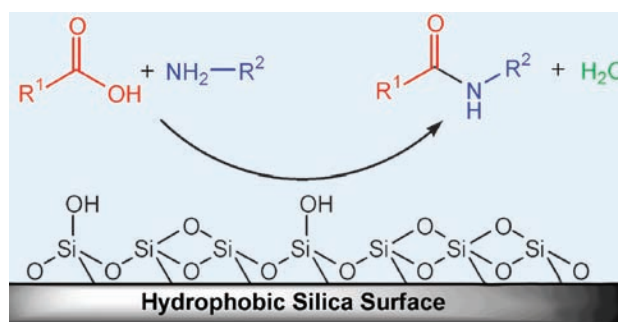
## Amide synthesis goes cheap, clean and simple

# Greening up pharmaceuticals

UK scientists have come up with a green method for synthesising amides, a fundamental reaction in the pharmaceutical industry, using a cheap and readily available material found lying around in labs.

James Clark and co-workers from the University of York developed a heterogeneous catalyst from silica gel, which is usually used as the stationary phase in column chromatography. They heated the silica gel to 700°C to activate it and then used it in a reaction to combine a carboxylic acid and an amine to make an amide. The only by-product was water, making the method cheaper, cleaner and less toxic than existing procedures. The catalyst remains active for a long time too, even after exposure to the atmosphere, and can be filtered for reuse.

Amides have been synthesised in



**Silica gel, used here to make amides, could be the key to a greener pharmaceutical industry**

**Reference**  
J W Comerford *et al.*, *Chem. Commun.*, DOI: 10.1039/b901581g

various ways over the years, but the methods are 'hazardous, complex and expensive', says Clark. 'Amide synthesis has been highlighted by the pharmaceutical industry as one of the most important targets for greening.'

Peter Dunn at Pfizer, Kent, UK, who is part of the industry group that identified amide synthesis as a prime target for greening, says:

'What I find most interesting about this research is that the authors have used standard silica, which can be found in any synthetic chemistry laboratory. They took a material that was just lying around in the lab and discovered that it can be easily converted to an effective catalyst for this important transformation.'

'Green chemistry should always challenge the more traditional chemistry community to reconsider established practices and to apply its skills and intelligence to design greener and more sustainable processes and products,' says Clark. 'We want to extend this particular type of chemistry to as wide a range of substrates and products as possible and then see where else we can apply the "simple is beautiful" and "complex isn't clever" philosophies.'

Mary Badcock

## Prostate cancer is easier to detect by combining biology with Raman scattering

# Working together to spot cancer

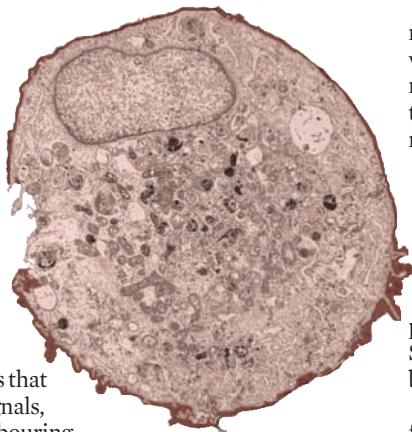
UK scientists have designed a method to detect prostate cancer using surface-enhanced resonance Raman scattering. Duncan Graham, from the University of Strathclyde in Glasgow, and his colleagues, combined the technique with a biological method called an enzyme-linked immunosorbent assay, or ELISA, to detect prostate specific antigen, whose elevated levels in serum indicate the cancer's presence.

ELISA is used to detect antigen levels in patients after prostate removal to ensure that all malignant tissue has been removed. Blood serum samples are fixed to a surface then a specific antibody is washed over the surface to bind to any antigen in the samples. Linked to the antibody is an enzyme dyed with a reagent that fluoresces when the antibodies bind to their antigens. This is normally

detected by fluorescence spectroscopy, but only one target at a time can be detected due to the large spectral overlap of dyes used for different targets.

Raman spectroscopy is used to investigate molecular bonding and can provide a unique vibrational 'fingerprint' for target molecules. For molecules that produce weak Raman signals, a highly scattering neighbouring surface such as gold can increase their response – this is surface-enhanced resonance Raman scattering (SERRS).

The team analysed antigen levels in human serum samples using ELISA, but in the final step used gold nanoparticles with SERRS to



**Elevated prostate specific antigen levels indicate the cancer's presence**

measure antigen concentration. They were able to detect picograms per millilitre antigen levels, lower than the current limit of nanograms per millilitre in cancer screening. Richard Van Duyn, an expert on SERRS from Northwestern University, Evanston, US, cautions that there are several other competing high-sensitivity approaches to measuring prostate specific antigen, such as surface plasmon resonance, but he agrees that SERRS has a 'bright future in solving biomedical problems'.

Graham says he hopes that in the future, he will be able to use SERRS to detect multiple proteins that indicate the presence of disease.

*Hilary Burch*

#### Reference

R Stevenson *et al*, *Analyst*, 2009, DOI: 10.1039/b902174d

# 42nd IUPAC CONGRESS

## Chemistry Solutions

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

Sponsored by  Schering-Plough

- Analysis & Detection
- Chemistry for Health
- Communication & Education
- Energy & Environment
- Industry & Innovation
- Materials including MC9 conference
- Synthesis & Mechanism

#### Deadlines:

Poster abstract – 5 June 2009

Early bird registration – 5 June 2009

Standard registration – 5 July 2009

Further information: [iupac2009@rsc.org](mailto:iupac2009@rsc.org)

Tel: +44 (0) 1223 432254 / 432380



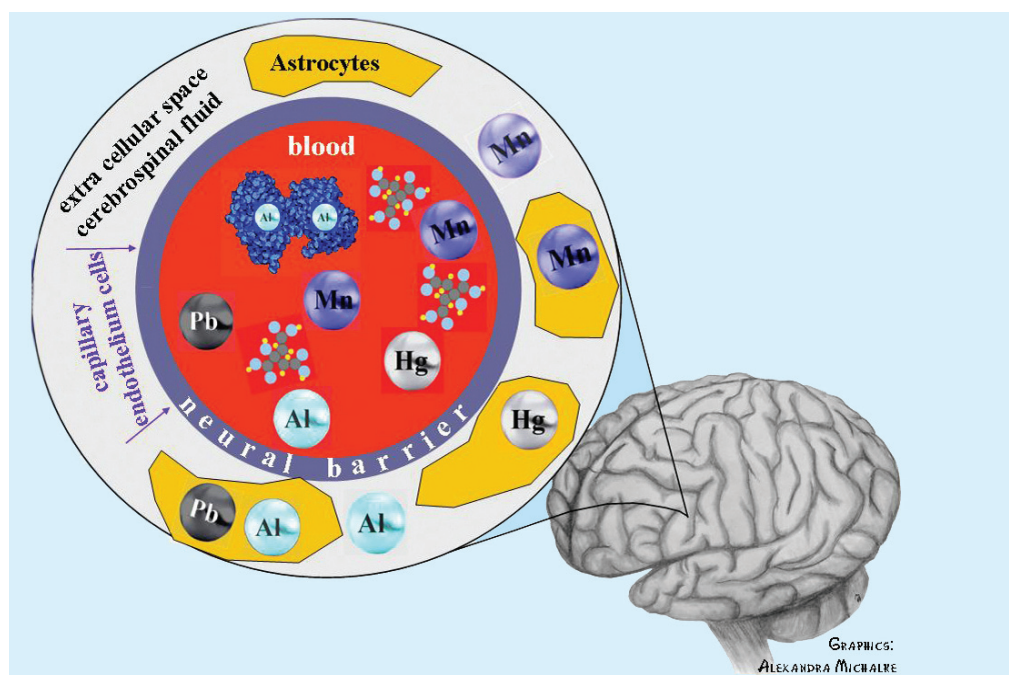
# Living longer, disease-free

Bernhard Michalke and colleagues at the Institute of Ecological Chemistry in Germany discuss our need for better methods to detect age-related diseases

Humans are living longer, particularly in industrialised countries. But with this extended lifespan comes an increased chance of suffering from age-related dementia and nervous system disorders such as Alzheimer's and Parkinson's diseases. These diseases severely reduce an individual's quality of life and are a heavy financial burden on national health systems. Any possible therapeutic cures have so far been limited.

The changes in the body's nervous system that can cause these diseases are the focus of neurotoxicology studies. Research has shown a link between exposure to metals such as aluminium, lead, manganese and mercury and nervous system degeneration. Elevated metal levels were found in the blood and brain samples of neurological disorder sufferers that had industrial manufacturing backgrounds. Exposure can happen in several ways, for example, aluminium is used as an additive in processed food and is present in cookware, contaminated water, medication and antiperspirants. Lead can be found in paints and water pipes in old houses, and glassware, some jewellery and tobacco. Occupational exposure occurs in lead smelters, lead refining and battery manufacturing. Exposure to elevated manganese levels occurs by mining and processing the element. Welding manganese alloys produces toxic fumes and dry-cell batteries and fireworks could contain manganese too. High mercury level sources include fish and dental amalgams. Occupational sources are combustion of fossil fuels or waste, the chloralkali industry, battery production, mercury alloys and polymer synthesis.

There have been many investigations into the metals' neurological and toxicological



effects, but the characterisation of their chemical forms (or trace element speciation) has not always been considered. Knowledge of trace element speciation can lead to a better understanding of how metals cross neural barriers and their potential role in causing disease in the human brain.

During the past few years, speciation analysis has become a valuable tool in highlighting neurotoxic chemical species and their pathways. Powerful techniques have been applied to human samples, mostly blood serum. More research is needed on other components that either transport species to the brain or are present in neuronal tissue or fluids. Some studies on cerebrospinal fluid and brain tissue have shown promise, but obtaining samples can be difficult. Results can also be hampered when the elements being studied are in low

**Trace element speciation analysis shows how metals cross the neural barrier to cause disease in the brain**

concentrations or their chemical forms are not stable. For example, in studies on the role of species such as aluminium-citrate, manganese-transferrin and manganese-citrate, forms in which the metals are able to cross the blood–brain barrier, in neurodegenerative diseases, even sample preparation, separation and storage time can change their identity or alter their concentration, making analytical quality control a challenge. These challenges and limitations illustrate that element speciation analysis in human body fluids is not an easy task. Until these problems are resolved, there will continue to be a lack of speciation data – data that could be the key to helping us live longer.

**Reference**  
B Michalke, S Halbach and V Nischwitz, *J. Environ. Monit.*, 2009, DOI: 10.1039/b817817h

Read more in *JEM Spotlight: Metal speciation related to neurotoxicity in humans'* in issue 5, 2009 of the Journal of Environmental Monitoring.

## A Break from the Routine?



- ✓ AVANCE™ III 400 MHz Ultrashield™ Plus Magnet
- ✓ Nanobay Console
- ✓ BBFO<sup>plus</sup> SmartProbe™
- ✓ Reliable Sample Automation
- ✓ TopSpin™ 2.1 Software

## • The Perfect Routine Package at a Price You Can Afford

- Easy to use - no specialist skills required
- Windows style, fully intuitive software featuring automated data acquisition and evaluation
- All the power you need right now - yet with guaranteed upgrade paths
- All-in-one SmartProbe - switch nuclei without switching probes!
- Small footprint magnet, ultracompact console for easy siting
- High throughput (24 hour operation) autosampling available
- Unrivalled reliability worldwide

## Tried and Trusted Routine NMR Solutions...

Contact us for more details: +44 (0)24 7685 5200  
[sales@bruker.co.uk](mailto:sales@bruker.co.uk) [www.bruker-biospin.com/organic\\_chemistry](http://www.bruker-biospin.com/organic_chemistry)

# Making logical connections

*Henry Rzepa tells Carl Saxton about the potential for creativity in both research and teaching activities*



**Henry Rzepa**

**Henry Rzepa is a professor of computational chemistry at Imperial College London, UK. His research focuses on modelling the shapes, properties and reactions of molecules and in presenting this information in internet-friendly ways.**

## Why did you decide to become a chemist?

We lived on a farm in Scotland. Once, my mother came down with flu and my father was away. I decided to make my mother a cup of tea. I had only a tenuous grasp of proportions and the resulting brew was close to one part water to 10 parts tea leaves. She drank it nonetheless. Thus encouraged, I started mixing anything I could find on the farm to see what would happen. By age 14, I had my own laboratory at home. After completing a synthesis of benzidine (nowadays firmly banned as being far too toxic) and reading a textbook on valence theory, the future course of my professional life was firmly set.

## What first got you interested in theoretical chemistry?

The textbook on valence theory I allude to above, but more firmly, after completing a PhD in physical organic chemistry and reaction mechanisms. I realised that all those linear free energy relationships I was measuring were not really telling me anything really fundamental about why the molecules I was studying behaved the way they did. I decided that only quantum mechanics was going to do this. At just the right time, Michael Dewar visited the department, and after his inspiring talk, I expressed an interest in working for him. A week later, a package weighing certainly more than a kilogram containing about 50 reprints for me to read arrived. I was hooked!

## What projects are you working on at the moment?

One area of research is about unravelling the origins of stereo- and chemoselectivity in metal-catalysed reactions. A good example is rationalisation of the heterotacticity in magnesium-catalysed lactide polymerisation, in terms of how isopropyl groups interact with phenyl faces and other groups.

The second area is the discovery and understanding of new forms of 'chiral aromaticity'. We, and others, have over the last decade shown how some aromaticities can originate from helical (twisted) arrangements of conjugated systems. The first glimmers started some 45 years ago, with the espousal of Möbius molecules by Heilbronner, but it's probably only in the last five years that lots of nice examples of this type of molecule have started to come to light.

The third theme is related to our aim of activating the internet for chemical application.

## What do you think the journal article will look like in twenty years' time?

Perhaps the biggest change I foresee is that the readership of the scientific article will not consist of just 'humans', but of what we refer to as 'machines'. The journal article will become semantically enabled, and software agents will be able to assimilate the article logically and infer logical connections to other knowledge. They will distil all this information down to a set of suggestions for the human to make those previously uncharted connections which we call discovery or indeed inspiration. As such, the boundaries and dimensions of what is now a well-defined article will soften and blur.

## What are your thoughts regarding RSC Prospect?

If I say it is ahead of its time, you must understand that I view it as very much central to our vision of the future. It is part of that semantically enabled vision I spoke about earlier. Currently, Prospect is still aimed squarely at human readers. But it's just a small step away from the full machine-human symbiosis that I mentioned before. If only all publishers were so innovative.

## You have been active in teaching for 31 years – how has the face of teaching changed?

Well, in many ways, students are still students! The very best were capable of astounding me 31 years ago with their enthusiasm and ability, and that still happens to this day. Observing how many students manage the transition from school to being able to cope with the real world in the four years they spend at university is one of the rewards of my job.

## Has there been a lot of interest in your lectures as podcasts?

The students certainly appreciate being able to replay lectures (in audio), and the enhanced visuals that podcasts can deliver. In one year, my podcasts made it into the iTunes top ten charts! However, preparing podcasts is very time-consuming, and only one other colleague has thus far tried it. So to some extent, we have really not achieved the critical mass of podcast materials in chemistry that would make the genre mainstream rather than just an oddity.

## If you weren't a scientist, what would you be?

Were it not for my total lack of any skills, I would have enjoyed being a composer.

# Essential elements

## Lab on a Chip goes YouTube™

Are you interested in watching the latest advances in microfluidics on video? The new *Lab on a Chip* YouTube™ video channel makes it possible by visualising all the latest scientific research in the field of miniaturisation. 'Many of the articles we receive for *Lab on a Chip* include video footage. These videos are currently captured on our journal website together with the scientific article, but we felt it was essential to share all this interesting information, not only with the scientists who regularly read *Lab on a Chip* but with the wider scientific community,' states Harp Minhas, editor of the journal.

One of the videos included

illustrates how researchers at the University of St Andrews, UK, use the unusual curving properties of laser beams to hurl microparticles and cells over walls. The scientists were looking into optically redistributing microparticles and cells between microwells.



'I think it is a great idea to establish such a video channel, in particular within the field of microfluidics where the vast majority of results are recorded

and presented as video files,' comments Jörg Baumgartl, who led the research. The associated article is published in *Lab on a Chip* as an advance article at [www.rsc.org/loc](http://www.rsc.org/loc).

'All scientists are keen to increase the visibility and impact of their work and this ties in with the RSC goal to communicate the chemical sciences as widely as possible and engage a wide audience,' adds Harp Minhas. 'Videos are a universal language and aid the understanding of scientific work on an international level. YouTube™ represents the perfect medium to help us achieve this goal.'

To find out more go to [www.youtube.com/labonachipvideos](http://www.youtube.com/labonachipvideos)

## Out and about

The Third *ChemComm* International Symposium on Organic Chemistry was held in February in China. The RSC partnered with three universities – Peking University, Sichuan University and the Shanghai Institute of Organic Chemistry – to host the three one-day meetings. With over 700 delegates attending and key speakers from across the world, the symposium was a huge success.

Sarah Thomas, editor of *ChemComm* comments: 'The lectures presented during the symposium were of outstanding quality and covered the whole breadth of organic chemistry from transition metal asymmetric catalysis, organocatalysis,

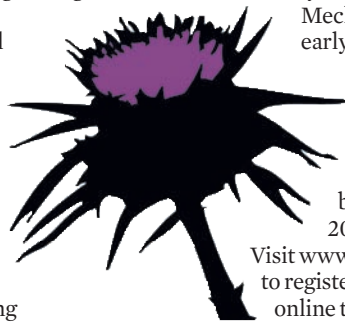
mechanistic studies to the synthesis of both natural and non-natural products.' Abstracts of the research presented at the symposium, and biographies of the presenters can be found at [www.rsc.org/chemcommsymposia](http://www.rsc.org/chemcommsymposia)

The RSC is also organising the 42nd IUPAC Congress which will be held in Glasgow, UK, in August. The programme features around 50 symposia, which will demonstrate the impact of the chemical sciences, highlighting

exciting innovations with an overall focus on 'Chemistry Solutions'. Key themes for this event are: Analysis & Detection, Chemistry for Health, Communication & Education, Energy & Environment, Industry & Innovation, Materials and

Synthesis & Mechanism. An early bird discount of £50 is available for those who register for the meeting before 5 June 2009.

Visit [www.iupac2009.org](http://www.iupac2009.org) to register your place online today!



*Chemical Science* (ISSN: 1478-6524) 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*, *Dalton Transactions*, *Organic & Biomolecular Chemistry*, *Journal of Materials Chemistry*, *Physical Chemistry Chemical Physics*, *Chemical Society Reviews*, *New Journal of Chemistry*, and *Journal of Environmental Monitoring*. *Chemical Science* can also be purchased separately. 2009 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](mailto:sales@rsc.org)

**Editor:** Elinor Richards

**Deputy editor:** Sarah Dixon

**Associate editors:** Celia Gitterman, Joanne Thomson

**Interviews editor:** Ruth Doherty

**Web editors:** Christina Ableman, Christina Hodkinson, Edward Morgan

**Essential elements:** Kathrin Hilpert and Christina Hartshorne

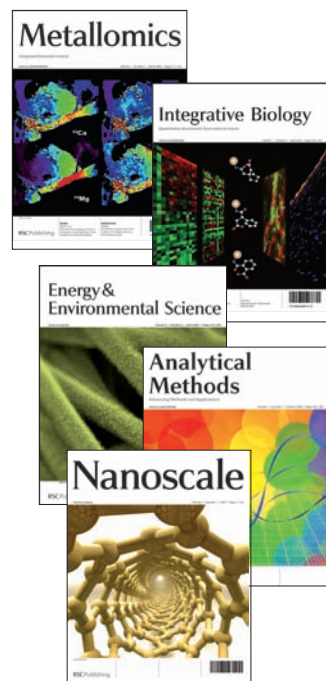
**Publishing assistant:** Jackie Cockrill

**Publisher:** Janet Dean

Apart from fair dealing for the purposes of research or private study for non-commercial purposes, or criticism or review, as permitted under the Copyright, Designs and Patents Act 1988 and the copyright and Related Rights Regulations 2003, this publication may only be reproduced, stored or transmitted, in any form or by any means, with the prior permission of the Publisher or in the case of reprographic reproduction in accordance with the terms of licences issued by the Copyright Licensing Agency in the UK. US copyright law is applicable to users in the USA.

## Did you know...

RSC Publishing offers FREE online institutional access for a number of new RSC journals. You could already be enjoying free access to *Metallomics* and *Integrative Biology*.



Don't miss out on the last months of *Energy & Environmental Science*'s free access period which expires at the end of 2009. In addition, RSC Publishing's two new journals, *Analytical Methods* and *Nanoscale*, will have free access until the end of 2010!

To register couldn't be easier. Just fill in our online form at [www.rsc.org/free\\_access\\_registration](http://www.rsc.org/free_access_registration) and start receiving the latest new journal issues today.

The Royal Society of Chemistry takes reasonable care in the preparation of this publication but does not accept liability for the consequences of any errors or omissions. The RSC is not responsible for individual opinions expressed in *Chemical Science*. Content does not necessarily express the views or recommendations of the RSC.

Royal Society of Chemistry: Registered Charity No. 207890.

## RSC Publishing