

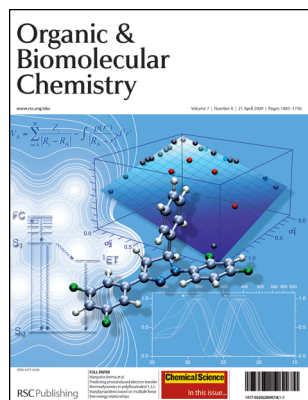
# Organic & Biomolecular Chemistry

An international journal of synthetic, physical and biomolecular organic chemistry  
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## IN THIS ISSUE

ISSN 1477-0520 CODEN OBCRAK 7(8) 1485–1736 (2009)

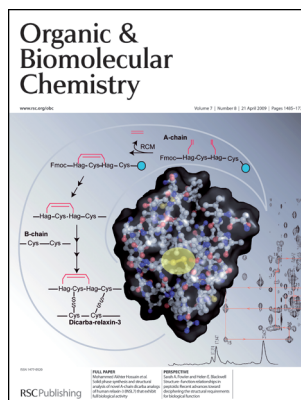


### Cover

See Manjusha Verma *et al.*, pp. 1536–1546.

The photophysical properties of polyfluorosubstituted pyrazolines were predicted based on free energy relationships with Hammett constants derived from theoretical electrostatic potentials at carbon nuclei.

Image reproduced by permission of Christoph Fahrni from *Organic & Biomolecular Chemistry*, 2009, **7**, 1536.



### Inside cover

See Mohammed Akhter Hossain *et al.*, pp. 1547–1553.

The intramolecular disulfide bond of human relaxin-3, an insulin-like peptide having potential applications in the treatment of obesity, was replaced with the physiologically stable dicarba bond.

Image reproduced by permission of John Wade from *Organic & Biomolecular Chemistry*, 2009, **7**, 1547.

## CHEMICAL SCIENCE

### C25

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

April 2009/Volume 6/Issue 4

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

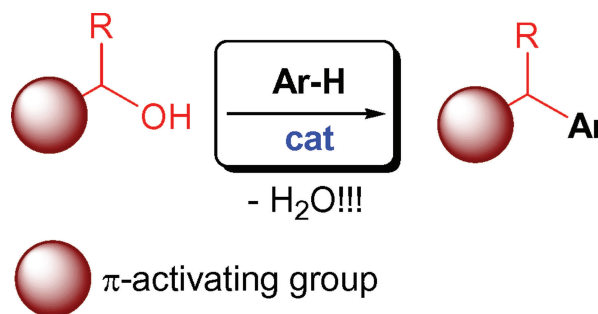
## EMERGING AREA

### 1501

#### $\pi$ -Activated alcohols: an emerging class of alkylating agents for catalytic Friedel–Crafts reactions

Marco Bandini\* and Michele Tragni

The use of  $\pi$ -activated alcohols under catalytic conditions is providing new solutions to old problems in Friedel–Crafts chemistry.



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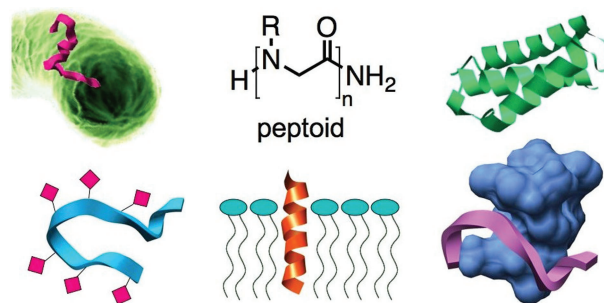
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1508

### Structure–function relationships in peptoids: Recent advances toward deciphering the structural requirements for biological function

Sarah A. Fowler and Helen E. Blackwell\*

Peptoids have emerged as a valuable class of foldamers for the study of biomolecular interactions, and hold promise as therapeutic agents. This perspective analyzes the importance of peptoid structure in the discovery of biologically active peptoids over the past five years.



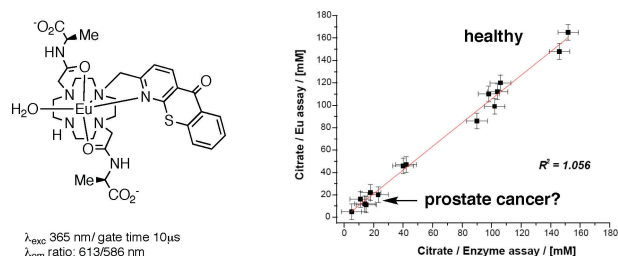
## COMMUNICATIONS

1525

### A europium luminescence assay of lactate and citrate in biological fluids

Robert Pal, David Parker\* and Leslie C. Costello

Ratiometric methods of analysis of Eu luminescence allow the determination of lactate and citrate in microlitre samples of human serum, urine or prostate fluids.

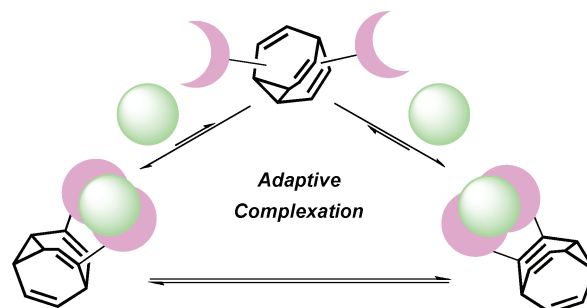


1529

### Dynamic supramolecular complexation by shapeshifting organic molecules

Alexander R. Lippert, Vasken L. Keleshian and Jeffrey W. Bode\*

The unique shapeshifting properties of a synthetic bisporphyrin bullvalene allow this molecule to adapt its structure in response to  $\text{C}_{60}$ , presenting a novel approach for the discovery of host–guest interactions.

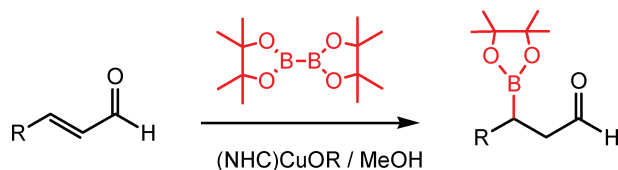


1533

### The selective catalytic formation of $\beta$ -boryl aldehydes through a base-free approach

Amadeu Bonet, Vanesa Lillo, Jesús Ramírez, M. Mar Díaz-Requejo and Elena Fernández\*

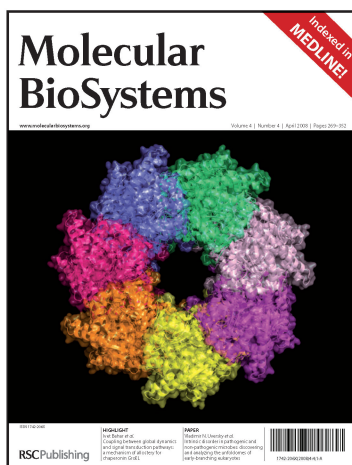
(NHC)CuOR (OR = OMe, O<sup>t</sup>Bu) and bis(pinacolato)diboron efficiently transform  $\alpha,\beta$ -unsaturated aldehydes into their corresponding  $\beta$ -organoboronate derivatives in the absence of base.



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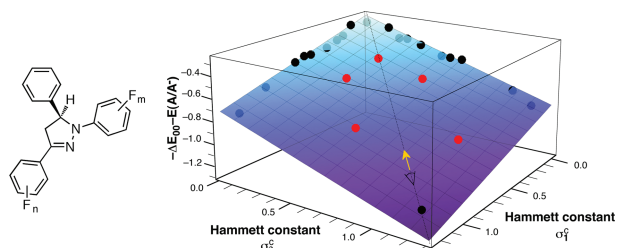
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1536

**Predicting the photoinduced electron transfer thermodynamics in polyfluorinated 1,3,5-triarylpyrazolines based on multiple linear free energy relationships**

Manjusha Verma, Aneese F. Chaudhry and Christoph J. Fahrni\*

Theoretical Hammett constants for polyfluoro-substituted benzenes were derived based on quantum chemical calculations and used to establish linear free energy relationships for predicting the photophysical properties of 1,3,5-triarylpyrazoline fluorophores.

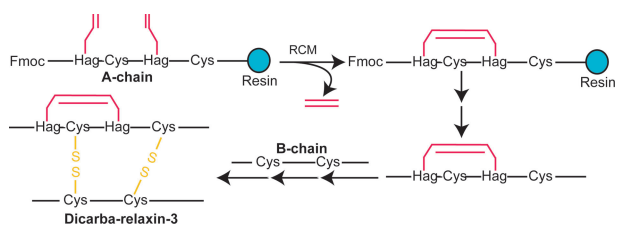


1547

**Solid phase synthesis and structural analysis of novel A-chain dicarba analogs of human relaxin-3 (INSL7) that exhibit full biological activity**

Mohammed Akhter Hossain, K. Johan Rosengren, Suode Zhang, Ross A. D. Bathgate, Geoffrey W. Tregear, Bianca J. van Lierop, Andrea J. Robinson and John D. Wade\*

An A-chain intramolecular dicarba bond analogue of human relaxin-3, with near-native structure and function, has been prepared.

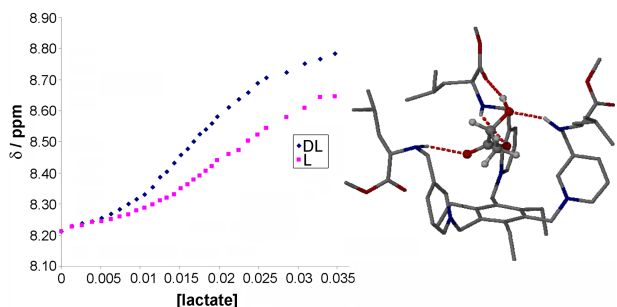


1554

**Enantioselective lactate binding by chiral tripodal anion hosts derived from amino acids**

Anna Barnard, Sara Jane Dickson, Martin J. Paterson, Adam M. Todd and Jonathan W. Steed\*

A chiral tripodal anion receptor discriminates between D- and L-lactate with up to *ca.* 70 % ee.

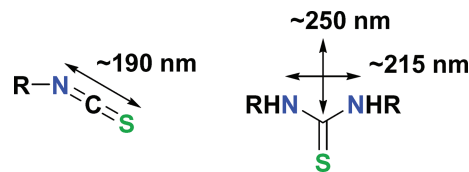


1562

**Thiourea and isothiocyanate – two useful chromophores for stereochemical studies. A comparison of experiment and computation**

Jacek Gawronski,\* Marcin Kwit and Pawel Skowronek

Thiourea and isothiocyanate chromophores give rise to CD spectra due to the exciton coupling mechanism. A comparison of experimental and TDDFT (B2LYP functional) calculated CD spectra allows determination of absolute configuration of these amine derivatives.

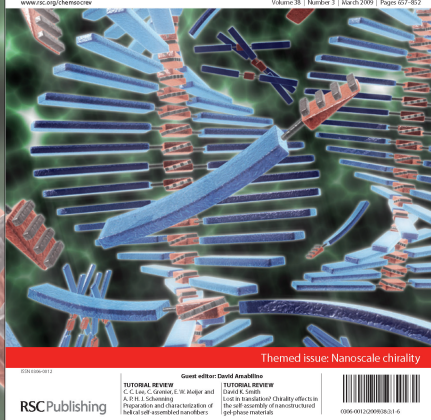


# Chem Soc Rev

Chemical Society Reviews

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Volume 38 | Number 3 | March 2009 | Pages 627-872



Themed issue: Nanoscale chirality

0300-0601(2)

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**EDITORIAL REVIEW**  
C. C. Lee, C. Grenier, E. W. Meijer and  
A. P. H. J. Schenning  
Preparation and characterization of  
helical self-assembled nanofibers

**TUTORIAL REVIEW**  
David B. Amabilino  
Loss of helical chirality in self-assembly  
of helical self-assembled nanofibers

0300-0601(2) 3  
www.rsc.org/chemsocrev

## Themed issue: Nanoscale chirality

Chirality in general is recognised widely as an area of great scientific and commercial interest. This themed issue contains reviews by experts who deal with everything from the theory of chiral systems, to their synthesis, self-assembly and processing; from characterisation using the most up to date techniques to their use in separation of enantiomers and their behaviour as materials.

### Reviews include:

#### Visualization of synthetic helical polymers by high-resolution atomic force microscopy

Jiro Kumaki, Shin-ichiro Sakurai and Eiji Yashima

#### Preparation and characterization of helical self-assembled nanofibers

Cameron C. Lee, Christophe Grenier, E. W. Meijer and Albertus P. H. J. Schenning

#### Lost in translation? Chirality effects in the self-assembly of nanostructured gel-phase materials

David K. Smith

#### Chiral expression at metal surfaces: insights from surface science techniques

R. Raval

#### Redox-triggered chiroptical molecular switches

James W. Canary

#### The chromatographic separation of enantiomers through nanoscale design

Raquel Sancho and Cristina Minguillón

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**David B. Amabilino**  
Materials Science Institute (CSIC)  
near Barcelona, Spain.

*"...This issue of Chemical Society Reviews gives an overview of the interest, importance, and applications of asymmetric chemical systems with features in the nanometre regime."*

020950

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[www.rsc.org/chemsocrev/nanoscalechirality](http://www.rsc.org/chemsocrev/nanoscalechirality)

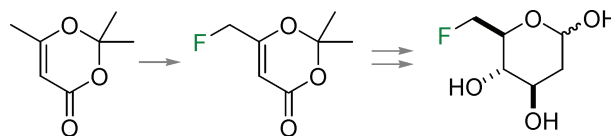
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1573

**An appraisal of oxoketene cycloaddition methodology for the synthesis of 2,6-dideoxysugars and fluorinated 2,6-dideoxysugars**

Christophe Audouard, Kim Bettaney (née Middleton), Châu T. Doan, Giuseppe Rinaudo, Peter J. Jarvis and Jonathan M. Percy\*

A fluorinated dioxinone provides an entry to 2,6-dideoxy-6-fluorosugars via oxoketene cycloaddition. Fluorinated and non-fluorinated systems are compared and contrasted by electronic structure calculations.

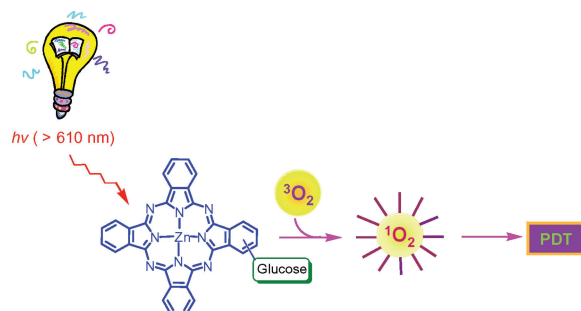


1583

**Effects of the number and position of the substituents on the *in vitro* photodynamic activities of glucosylated zinc(II) phthalocyanines**

Jian-Yong Liu, Pui-Chi Lo, Wing-Ping Fong and Dennis K. P. Ng\*

A novel series of tetraethylene-glycol-linked glucosylated zinc(II) phthalocyanines have been synthesised and characterised. The effects of the number and position of these substituents on their *in vitro* photocytotoxicity have also been examined.

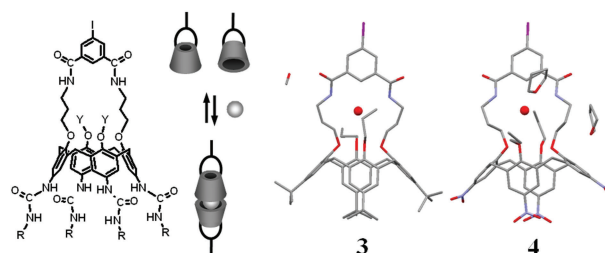


1592

**Tetra-urea calix[4]arenes 1,3-bridged at the narrow rim**

Ganna Podoprygorina, Michael Bolte and Volker Böhmer\*

Tetra-urea calix[4]arenes symmetrically bridged by an isophthalamide handle have been synthesized and shown to form hydrogen bonded dimers with  $D_2$ -symmetry in apolar solvents. Two intermediates were characterized by a crystal structure.

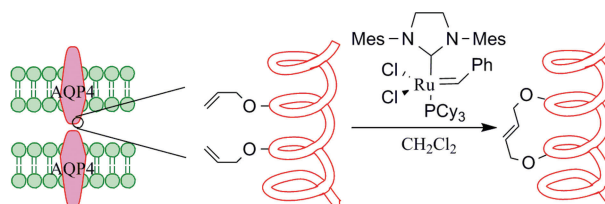


1599

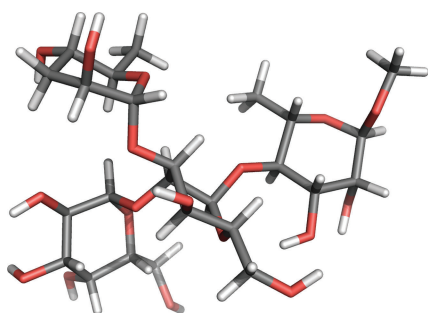
**Synthesis of cyclic peptide analogues of the  $3_{10}$  helical Pro138-Gly144 segment of human aquaporin-4 by olefin metathesis**

Øyvind Jacobsen,\* Jo Klaveness, Ole Petter Ottersen, Mahmood Reza Amiry-Moghaddam and Pål Rongved

Conformationally restrained cyclic peptides modelled on the  $3_{10}$  helical Pro138-Gly144 segment of the water channel aquaporin-4 (AQP4) postulated to mediate adhesive interactions between AQP4 tetramers were synthesised by olefin metathesis.



1612



### Synthesis of and molecular dynamics simulations on a tetrasaccharide corresponding to the repeating unit of the capsular polysaccharide from *Salmonella enteritidis*

Johan D. M. Olsson, Jens Landström, Jerk Rönnols, Stefan Oscarson and Göran Widmalm\*

The synthesis of a tetrasaccharide related to the repeating unit of *S. enteritidis* capsular polysaccharide is presented. A molecular dynamics simulation of the oligosaccharide shows inherent high flexibility and population of several conformational states.

1619



Independent rotation

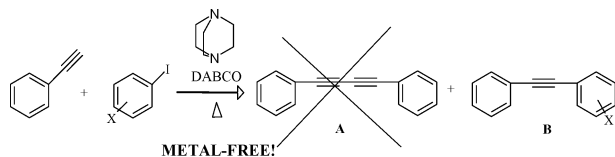
Correlated rotation

### Steric effects which determine the conformational preferences and stereodynamic processes of aryl fluorenyl ketones

Daniele Casarini,\* Lodovico Lunazzi and Andrea Mazzanti\*

Aryl fluorenyl ketones have been investigated by dynamic NMR, DFT calculations and X-ray diffraction. Independent rotation of the aryl rings is changed into correlated rotation by modification of the *ortho*-substituents of the phenyl ring.

1627

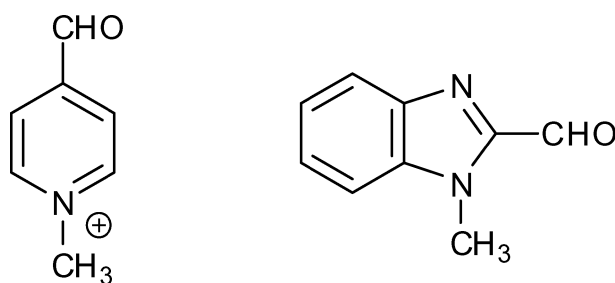


### Efficient solvent- and metal-free Sonogashira protocol catalysed by 1,4-diazabicyclo(2.2.2) octane (DABCO)

Rafael Luque\* and Duncan J. Macquarrie

Time for metal-free couplings? DABCO can efficiently promote Sonogashira couplings in the absence of transition metal catalysts providing very good yields and selectivities to cross-coupling products.

1633



### Hidden signatures: new reagents for developing latent fingerprints

M. John Plater,\* Paul Barnes, Lauren K. McDonald, Sandy Wallace, Nia Archer, Thomas Gelbrich, Peter N. Horton and Michael B. Hursthouse

New reagents for the development of latent fingerprints have been studied which possess an aldehyde moiety attached to a pyridinium or a benzimidazole nucleus. The proposed reaction of the pyridinium salt reagents with amino acids is compared to a biochemical system that interconverts aldehydes with amines.



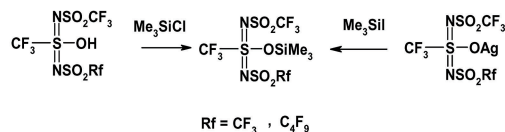
1642

**New kinds of organic superacids.  
Bis(perfluoroalkylsulfonylimino)trifluoromethanesulfonic acids and their trimethylsilyl esters**

Anna G. Posternak, Romute Yu. Garlyauskayte,\*  
Vitalij V. Polovinko, Lev M. Yagupolskii and  
Yurii L. Yagupolskii

An attempt to estimate the strength of bis(perfluoroalkylsulfonylimino)-trifluoromethanesulfonic acids among various sulfonic acids was performed based on the  $^{29}\text{Si}$  NMR data of the corresponding trimethylsilyl esters.

|               | $\text{R}-\text{S}(\text{O})_2\text{OH}$ | $\text{Rf}-\text{S}(\text{O})_2\text{OH}$ | $\text{CF}_3-\text{S}(\text{O})_2\text{OH}$ |
|---------------|--|---|---|
| $\text{pK}_a$ | $-2 \div -3$                             | -6  | -11.5                                       |
| $-\text{H}_0$ | $7 \div 8$                               | 14  | 25  |

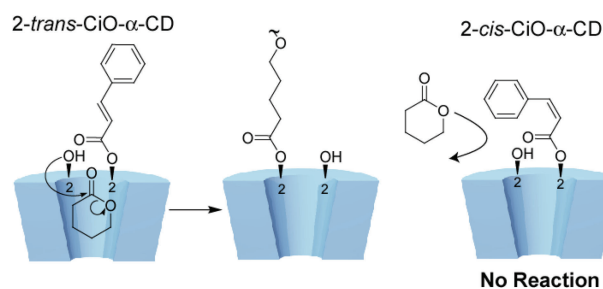


1646

**Switching of polymerization activity of  
cinnamoyl- $\alpha$ -cyclodextrin**

Motofumi Osaki, Yoshinori Takashima,  
Hiroyasu Yamaguchi and Akira Harada\*

Cinnamoyl  $\alpha$ -cyclodextrin ( $\alpha$ -CD) initiated polymerization of  $\delta$ -valerolactone in high yield. The polymerization activity was switched by photoisomerization of the cinnamoyl group attached to the rim of  $\alpha$ -CD.

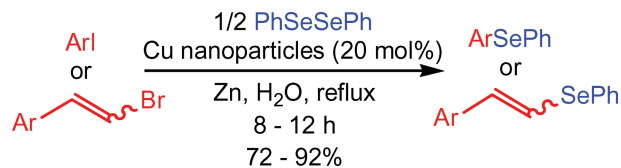


1652

**Copper nano-catalyst: sustainable phenyl-selenylation of  
aryl iodides and vinyl bromides in water under ligand free conditions**

Amit Saha, Debasree Saha and Brindaban C. Ranu\*

Copper nanoparticles have been demonstrated to be very efficient at catalysing the phenyl-selenylation of aryl iodides and vinyl bromides, producing aryl- and vinyl-selenides in water without the requirement for any ligand.

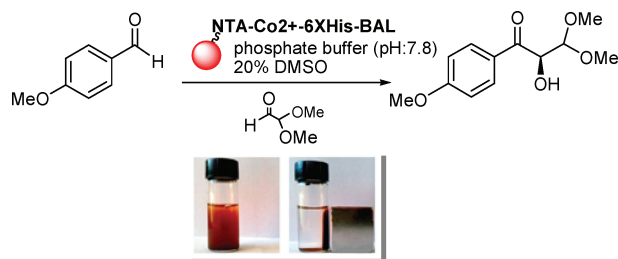


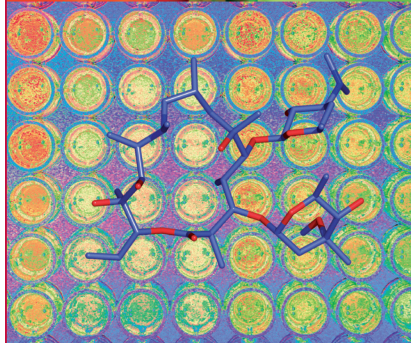
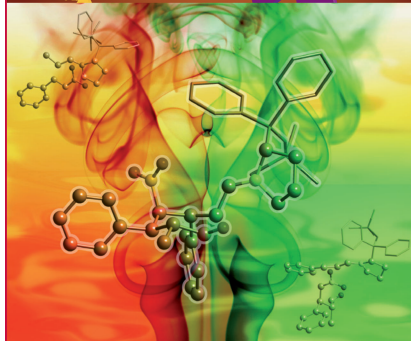
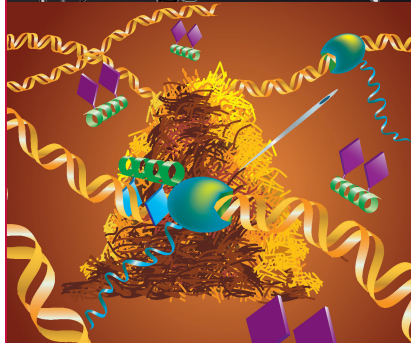
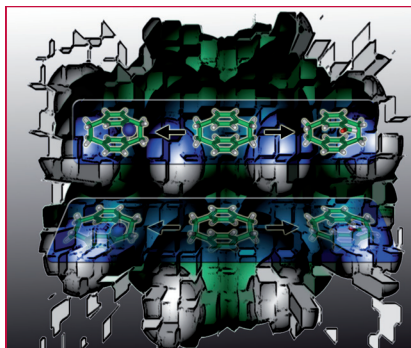
1658

**Carboligation reactions with benzaldehyde lyase  
immobilized on superparamagnetic solid support**

Ş. Betül Sopacı, İlke Şimşek, Bilsen Tural, Mürvet Volkan  
and Ayhan S. Demir\*

6XHis-tagged benzaldehyde lyase immobilized on surface-modified magnetic particles, a simple and convenient heterogeneous biocatalyst comparable to the free enzyme.





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### Perspective:

#### Chemical approach toward efficient DNA methylation analysis

Akimitsu Okamoto, *Org. Biomol. Chem.*, 2009, **7**, 21

DOI: 10.1039/b813595a

### Emerging Area:

#### Mechanistic approaches to palladium-catalyzed alkene difunctionalization reactions

Katrina H. Jensen and Matthew S. Sigman, *Org. Biomol. Chem.*, 2008, **6**, 4083

DOI: 10.1039/b813246a

### Communications:

#### 3- and 5-Functionalized BODIPYs via the Liebeskind-Srogl reaction

Junyan Han, Oswaldo Gonzalez, Angelica Aguilar-Aguilar, Eduardo Peña-Cabrera and Kevin Burgess, *Org. Biomol. Chem.*, 2009, **7**, 34

DOI: 10.1039/b818390b

#### Stereoselective synthesis of the hormonally active (25S)- 7-dafachronic acid, (25S)- 4-dafachronic acid, (25S)-dafachronic acid, and (25S)-cholestenoic acid

René Martin, Frank Däbritz, Eugeni V. Entchev, Teymuras V. Kurzchalia and Hans-Joachim Knölker, *Org. Biomol. Chem.*, 2008, **6**, 4293

DOI: 10.1039/b815064h

### Papers:

#### Cyclic tetraureas with variable flexibility – synthesis, crystal structures and properties

Denys Meshcheryakov, Françoise Arnaud-Neu, Volker Böhmer, Michael Bolte, Julien Cavaleri, Véronique Hubscher-Bruder, Iris Thondorf and Sabine Werner  
*Org. Biomol. Chem.*, 2008, **6**, 3244

DOI: 10.1039/b808773c

#### Recognition and discrimination of DNA quadruplexes by acridine-peptide conjugates

James E. Redman, J. M. Granadino-Roldán, James A. Schouten, Sylvain Ladame, Anthony P. Reszka, Stephen Neidle and Shankar Balasubramanian,  
*Org. Biomol. Chem.*, 2009, **7**, 76

DOI: 10.1039/b814682a

#### Indium and zinc-mediated Barbier-type addition reaction of 2,3-allenals with allyl bromide: an efficient synthesis of 1,5,6-alkatrien-4-ols

Wangqing Kong, Chunling Fu and Shengming Ma, *Org. Biomol. Chem.*, 2008, **6**, 4587

DOI: 10.1039/b812869c

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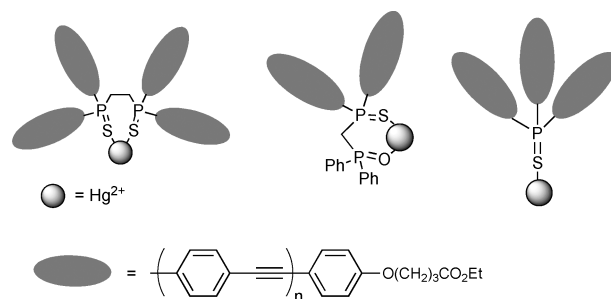
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1665

### Highly selective and sensitive Hg<sup>2+</sup> fluorescent sensors based on a phosphane sulfide derivative

Minh-Huong Ha-Thi, Maël Penhoat, Véronique Michelet\* and Isabelle Leray\*

A series of fluorescent sensor molecules based on a phosphane sulfide derivative was synthesized. These fluorescent molecular sensors exhibit very low detection limits in CH<sub>3</sub>CN/H<sub>2</sub>O mixture (80/20 v:v) and excellent sensitivity to Hg<sup>2+</sup> over other potentially interfering cations.

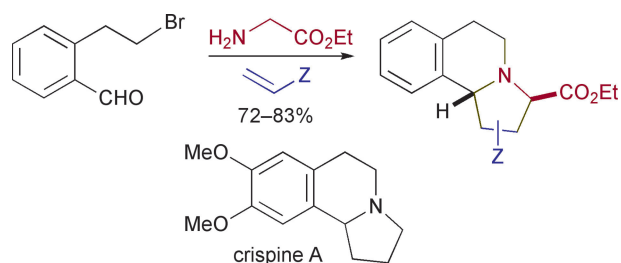


1674

### Cascade condensation, cyclization, intermolecular dipolar cycloaddition by multi-component coupling and application to a synthesis of (±)-crispine A

Iain Coldham,\* Samareh Jana, Luke Watson and Nathaniel G. Martin

Addition of amino-acids or amino-esters to halo-aldehydes gives azomethine ylides that undergo dipolar cycloaddition.

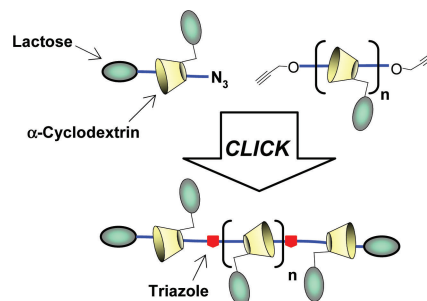


1680

### Synthesis and biological evaluation of multivalent carbohydrate ligands obtained by click assembly of pseudo-rotaxanes

Martin Chwalek, Rachel Auzély and Sébastien Fort\*

Carbohydrate appended oligorotaxanes with adjustable ligand densities have been prepared by assembling  $\alpha$ -cyclodextrin-based pseudo-rotaxanes through “click chemistry”.

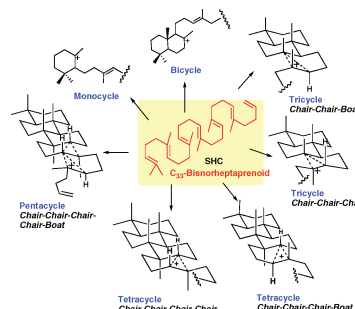


1689

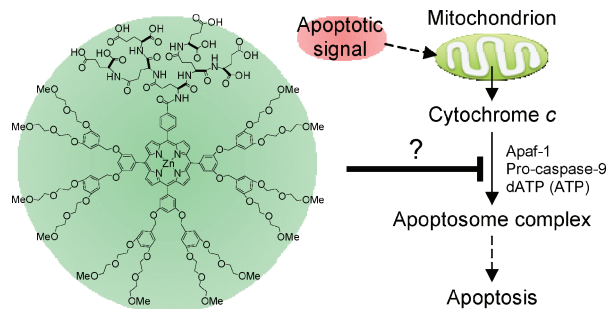
### Cyclization cascade of the C<sub>33</sub>-bisorheptaprenoid catalyzed by recombinant squalene cyclase

Jun Cheng and Tsutomu Hoshino\*

Incubation of C<sub>33</sub>-bisorheptaprenoid with SHC yielded mono-, bi-, tri-, tetra- and pentacyclic products. However, no hexacyclic product was generated.



1700

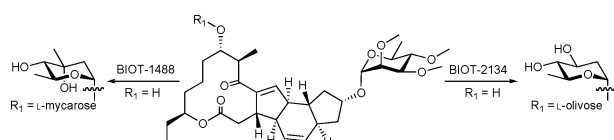


### Cytochrome *c*-binding “*proteo-dendrimers*” as new types of apoptosis inhibitors working in HeLa cell systems

Hideki Azuma,\* Yuuka Yoshida, Dharam Paul, Satoshi Shinoda, Hiroshi Tsukube and Takeshi Nagasaki

The suppressive effects of synthetic dendrimers on mitochondrial apoptosis were first demonstrated in human epithelial carcinoma HeLa cells.

1705

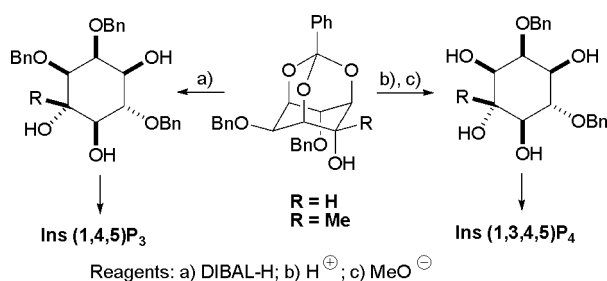


### Glycosylation engineering of spinosyn analogues containing an L-olivose moiety

Sabine Gaisser, Isabelle Carletti, Ursula Schell, Paul R. Graupner, Thomas C. Sparks, Christine J. Martin and Barrie Wilkinson\*

Spinosyn analogues containing L-olivose derived by overexpression of L-mycarose precursor biosynthesis genes.

1709

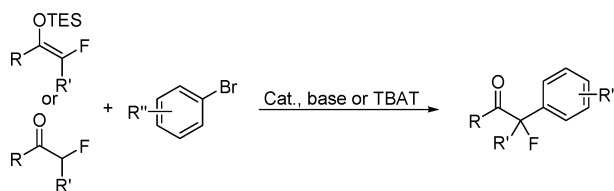


### Regioselective deprotection of orthobenzoates for the synthesis of inositol phosphates

Joanna M. Swarbrick, Samuel Cooper, Geert Bultynck and Piers R. J. Gaffney\*

The reduction of asymmetrical *myo*-inositol orthobenzoates using DIBAL-H and the syntheses of 4-*C*-methyl-*myo*-inositol 1,4,5-triphosphate and 4-*C*-methyl-*myo*-inositol 1,3,4,5-tetrphosphosphate are described.

1716



### Pd-catalyzed arylation of silyl enol ethers of substituted $\alpha$ -fluoroketones

Yong Guo, Brendan Twamley and Jean'ne M. Shreeve\*

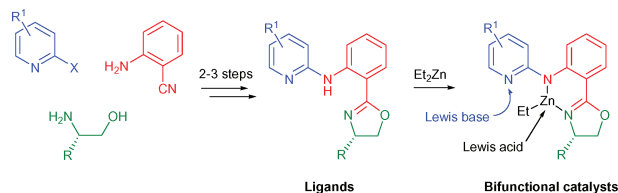
$\alpha$ -Fluoro- $\alpha$ -aryl-ketones were synthesized by Pd-catalyzed cross-coupling of aryl bromides with either  $\alpha$ -fluoroketones or their corresponding silyl enol ethers. Good functional tolerance was achieved when silyl enol ethers were used.

1723

## The synthesis of new oxazoline-containing bifunctional catalysts and their application in the addition of diethylzinc to aldehydes

Vincent Coeffard, Helge Müller-Bunz and Patrick J. Guiry\*

A set of new oxazoline-containing bifunctional catalysts has been prepared and applied in the asymmetric addition of diethylzinc to aldehydes (*ee* values up to 68%).




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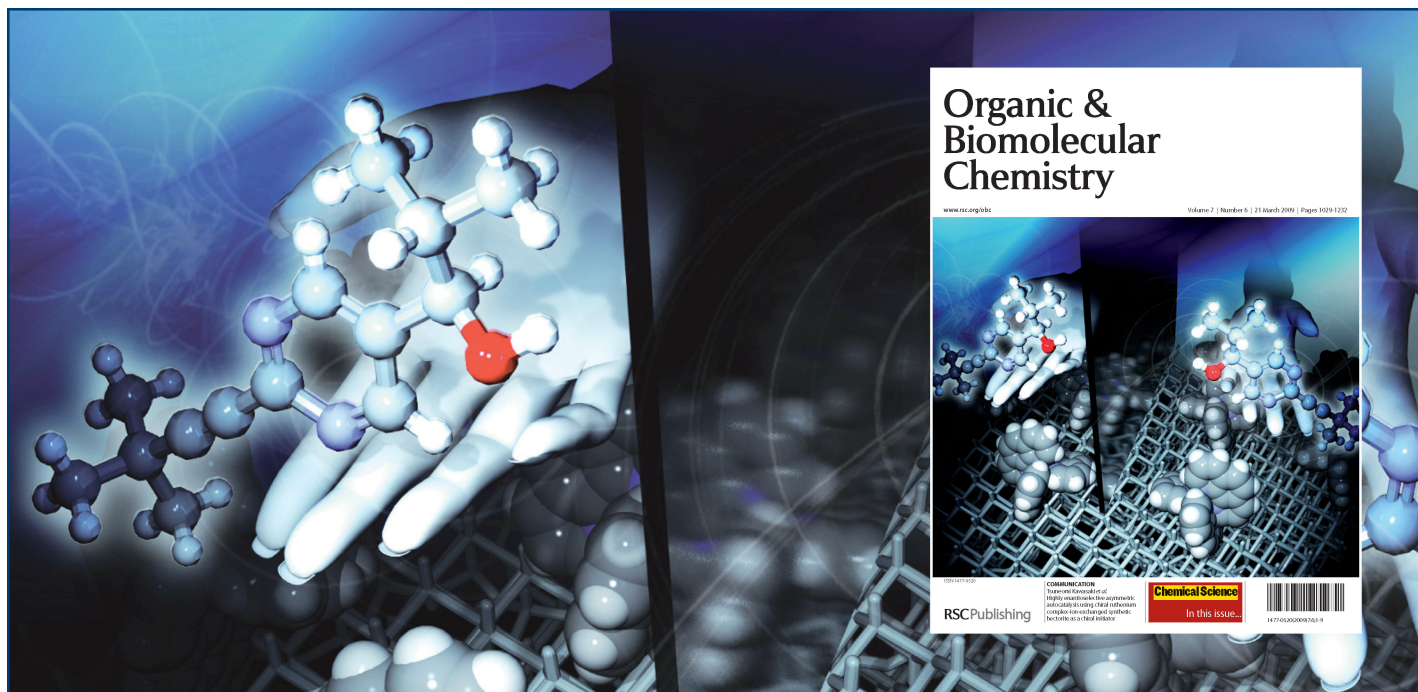
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Yoshihiro Matano and Hiroshi Imahori, *Org. Biomol. Chem.*, 2009, DOI: 10.1039/b819255n

### Emerging Area:

#### Metal-catalysed halogen exchange reactions of aryl halides

Tom D. Sheppard, *Org. Biomol. Chem.*, 2009, DOI: 10.1039/b818155a

### Communication:

#### Highly enantioselective asymmetric autocatalysis using chiral ruthenium complex-ion-exchanged synthetic hectorite as a chiral initiator

Tsuneomi Kawasaki, Toshiki Omine, Kenta Suzuki, Hisako Sato, Akihiko Yamagishi and Kenso Soai, *Org. Biomol. Chem.*, 2009, DOI: 10.1039/b823282b

### Paper:

#### Ruthenium-based metallacrown complexes for the selective detection of lithium ions in water and in serum by fluorescence spectroscopy

Sébastien Rochat, Zacharias Grote and Kay Severin, *Org. Biomol. Chem.*, 2009, DOI: 10.1039/b820592b

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# Chemical Science

An artificial vascular system has been made using candy floss as a template

## Making capillaries with candy floss

Candy floss (also known as cotton candy) has been used by US scientists to create a web of microscopic tubes to mimic the capillary network that carries blood to human tissue.

Leon Bellan at Cornell University's Nanobiotechnology Center, Ithaca, and colleagues, mimicked the capillary network structure by sticking two sugar rods to a candy floss ball. They poured a molten polymer over the candy floss, left it to solidify, then dissolved the sugar, leaving a complex network of channels connecting two larger inlet and outlet channels. They then injected fluorescently labelled blood into the system and followed its progress using a video fluorescence microscope. They found that the blood flowed through as it would in a real system.

Bellan's method addresses a limitation in tissue engineering: how to make an artificial vascular system for the new tissue. Since blood can only diffuse a few hundred micrometres from a capillary, organs need these networks to deliver oxygen and nutrients to every



cell. His technique is cheaper and less time consuming than existing methods for making the networks, such as layer-by-layer 2D structure stacking or 3D printing, where templates for growing cells are built up.

Candy floss is an ideal template as it is cheap, non-toxic, water soluble

**Molten polymer was poured over candy floss to create a capillary network model**

**Reference**  
L M Bellan *et al*, *Soft Matter*, 2009, DOI: 10.1039/b819905a

and sticky. The stickiness allows junctions between the sugar rods and the candy floss to form easily. The only equipment required is a candy floss machine, which can be purchased for as little as \$40 (approximately £30), says Bellan.

'Finding inspiration from something in everyday life is very clever,' says Jeff Borenstein, director of the Biomedical Engineering Center at Draper Laboratory, Cambridge, US. 'It reminds me of how the pioneering tissue engineer, Jay Vacanti, was inspired to create 3D scaffolds for tissue engineering by observing the structure of seaweed while on a Cape Cod beach.'

Bellan says that potential applications for his method, aside from helping to grow organs in the laboratory, could include making self-healing polymers that can fracture and heal, over and over again in the same place. 'The simplicity and low cost of this new fabrication technique should render many applications of 3D microfluidic networks commercially viable,' he says. *James Hodge*

## In this issue

### Fighting MRSA with ionic liquids

Ionic liquids could be used to tackle hospital acquired infections

### Hydrogen storage steps up a gear

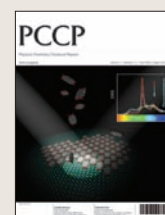
Improved storage takes us closer to hydrogen fuelled cars

### The growth of nanotoxicology

This month's Instant insight looks at analytical techniques used to assess nanotechnology's effects on health

### Creating a new world

Mukund Chorghade talks about his fascination with natural products and their role in India's future



A snapshot of the latest developments from across the chemical sciences

# Research highlights

Aquatic organisms' feeding behaviour can be affected by ionic liquids

## Ionic liquids put zebra mussels off their food

Non-lethal doses of ionic liquids can have a significant effect on aquatic ecosystems, claim US scientists.

Ionic liquids are green alternatives to the volatile organic solvents that are released into the environment as a result of agriculture and manufacturing. But their solubility in water means that they can contaminate aquatic environments. Knowledge of their toxicity in these environments is limited, but even less is known about their non-lethal effects on aquatic organisms.

Now, David Costello and colleagues from the University of Notre Dame have studied how ionic liquids affect aquatic organisms' feeding rates as well as their survival.

The team looked at zebra mussels, which feed by filtration and can tolerate high doses of ionic liquids. They fed the mussels algae and exposed them to six different ionic liquids. They found that while changing the heterocyclic base of the



ionic liquid's cation had no effect, increasing the length of its alkyl chain increased toxicity and decreased the mussels' feeding rate. 'A reduction in algal consumption could allow

**Ionic liquids decreased the zebra mussel's feeding rate**

increases in algal populations that are resistant to ionic liquids,' says Costello.

'The work is a valuable contribution to the knowledge base that the scientific community is generating on potential harmful effects that will have to be considered if ionic liquids are to be used on a large scale,' says Johannes Ranke, an expert in the environmental risk assessment of ionic liquids, from the University of Bremen, Germany.

Costello says he hopes that within 5 to ten years, he will find more environmentally friendly solvents and that green solvents will be used more in general. He is currently investigating the nutrient cycle (the transfer of nutrients from one part of an ecosystem to another) in invasive species and contaminants and studying how contaminants affect nitrogen and phosphorus movement in the environment.

Ben Merison

### Reference

D M Costello, L M Brown and G A Lamberti, *Green Chem.*, 2009, DOI: 10.1039/b822347e

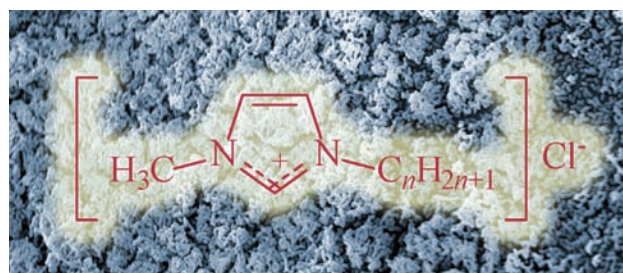
Ionic liquids could be used to tackle hospital acquired infections

## Fighting MRSA with ionic liquids

Hospital cleaners may one day use ionic liquids to clean wards. Brendan Gilmore and co-workers at the Queen's University, Belfast, UK, have shown that the compounds are effective antibacterial agents that can be used to break down microbial biofilms, a cause of hospital acquired infections such as MRSA.

Ionic liquids are low temperature molten salts formed from cations and anions. While ionic liquids must be tested for environmental toxicity before they can be used as safer alternatives to industrial solvents, Gilmore is using their toxicity for the benefit of human health. 'Altering the cation and anion pairing allows you to tune the toxicity,' says Gilmore.

Gilmore tested the effects of 1-alkyl-3-methylimidazolium chloride ionic liquids on the



bacterial biofilms of several pathogens including methicillin-resistant *Staphylococcus aureus* and *Escherichia coli*. The team found that antibiofilm potency increased with the length of the alkyl chain. Biofilms are bacterial communities that enclose themselves in a protective polymer. They are more resistant to antibiotics or other sterilisation methods than their free-swimming counterparts.

**1-Alkyl-3-methylimidazolium chloride ionic liquids were effective against *Staphylococcus aureus* and *E. coli* bacterial biofilms**

### Reference

L Carson *et al*, *Green Chem.*, 2009, DOI: 10.1039/b821842k

'Resistance to antimicrobials is an increasing global threat to public health,' says Jan Michiels, an expert in biofilms at the Catholic University of Leuven, Belgium. Ionic liquids could be applied to a surface already hosting a biofilm to help sterilise it, but Gilmore says he hopes that ionic liquids will be used to coat surfaces to prevent biofilms forming.

According to Gilmore, the advantages might not be limited to the health sector. Microbial biofilms can foul pipes in industrial machinery, and marine antifouling – a coating painted on to the hull of ships – could be another potential application.

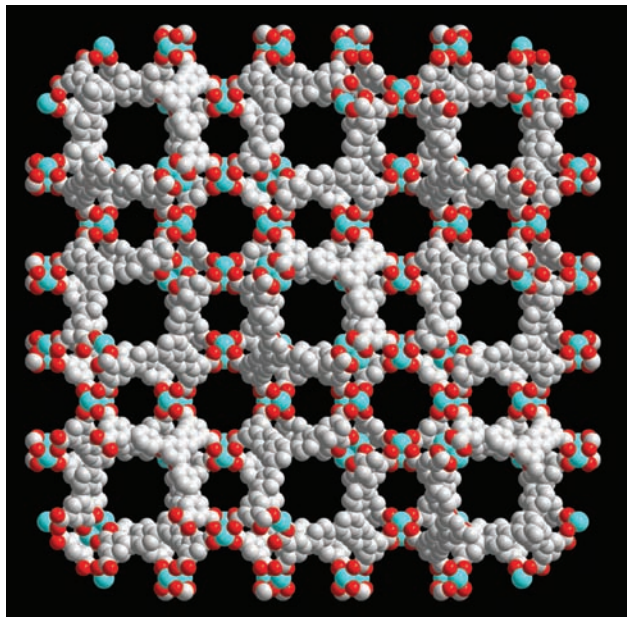
Gilmore's team is currently working on novel ionic liquids with improved antimicrobial and antibiofilm activities.

Russell Johnson



# Improved storage takes us closer to hydrogen fuelled cars

## Hydrogen storage steps up a gear

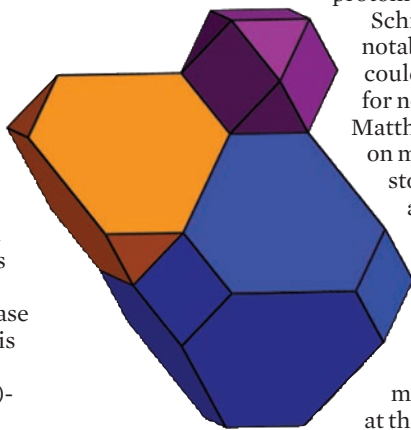


Martin Schröder at the University of Nottingham, UK, and colleagues, have made a porous solid for hydrogen storage with significantly increased hydrogen capacity. Ping Wang and colleagues at the Chinese Academy of Sciences, Shenyang, have discovered that hydrogen release from ammonia borane, a material with high hydrogen storage capability, can be accelerated by mechanical milling with magnesium hydride.

'Hydrogen represents an important potential energy source with zero carbon emissions at the point of use,' explains Schröder. The main barrier to its use as a vehicle fuel is the enormous storage volumes needed when it is carried in its molecular form, so how to increase capacity in any storage material is a key issue.

Schröder's solid is a copper(II)-based metal-organic polymer made up of three polyhedral cages that fit together to provide a hollow framework. The polymer can take up 10 wt% hydrogen at 77 bar and 77 Kelvin. 'This uptake is amongst the highest to date for this class of porous material and is a major contribution to

**The cage arrangement promotes hydrogen adsorption at high and low pressures maximising the obtainable storage capacity. An example of how the cages fit together is shown below**



### References

- 1 Y Yan *et al.*, *Chem. Commun.*, 2009, 1025 (DOI: 10.1039/b900013e)
- 2 X Kang *et al.*, *Phys. Chem. Chem. Phys.*, 2009, DOI: 10.1039/b820401b

the 2010 target of 6.5 wt% for a whole storage system set by the US Department of Energy,' says Schröder.

Another key requirement for hydrogen storage systems is fast hydrogen charge and discharge rates to meet consumer expectations for refuelling. Wang worked with ammonia borane, which has exceptional hydrogen storage capacity but a slow release rate. His milling technique speeds up hydrogen release. More than 8 wt% hydrogen can be released within four hours at 100°C, the lowest temperature obtained in any hydride system tested so far, says Wang. Low temperatures are important for controlling hydrogen release and spent fuel regeneration.

'Promoting hydrogen release by mechanically milling solid ammonia borane is not new,' explains Wang, 'but our studies show a completely different chemical activation mechanism that doesn't take place via alkali metal amidoboranes.' According to Wang, hydrogen is released through a destabilising solid phase reaction between the hydridic  $H^{\delta-}$  in magnesium hydride and the protonic  $H^{\delta+}$  in ammonia borane.

Schröder's structure is notable and its properties could help guide the search for new systems, says Matthew Rosseinsky, an expert on materials for energy storage and generation at the University of Liverpool, UK.

Schröder says that the next challenge is to increase the strength of hydrogen binding within his material to enable storage at the higher, more ambient temperatures needed for automobile-based applications. For Wang, understanding how magnesium hydride destabilises ammonia borane is key to designing systems with better capacity and kinetic performance. *Janet Crombie*

## News in brief

### This month in Chemical Technology

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## Glycopolymer spheres may be better living cell mimics and drug delivery vessels

# Polymer's coats multi-task in drug delivery

Polymer spheres with a sugar coating on the outside and plastic coating on the inside have been made by European scientists. This gives them dual functionality to target and deliver drugs.

Helmut Schlaad from the Max Planck Institute of Colloids and Interfaces, Potsdam, and colleagues from Germany and Switzerland made the spheres by dissolving glycosylated polybutadiene–poly(ethylene oxide) block copolymers in water. When dissolved, the copolymers spontaneously formed hollow colloids called vesicles with a glucose coating on the outside and a poly(ethylene oxide) coating on the inside.

The polymer vesicles could be used as living cell mimics or drug delivery vessels. Thanks to their adjustable properties – stability,



fluidity and dynamics – they could be better models for biomedical research than vesicles made from the phospholipids found in cells. Usually, the coatings on both sides of a vesicle's membrane are the same. As the outside and inside of Schlaad's vesicles are different, it may be possible to assign different tasks to each side. 'It would be very interesting to have vesicles with an asymmetric membrane for many

**The plastic and sugar coatings give the vesicles dual functionality to target and deliver drugs**

**Reference**  
H Schlaad *et al*, *Chem. Commun.*, 2009, 1478 (DOI: 10.1039/b820887e)

applications, especially in life sciences,' says Schlaad.

For example, they could be used to target drugs and biomolecules to injured or cancerous tissues, says René Roy, an expert in carbohydrate chemistry and glycobiology at the University of Québec, Montréal, Canada. 'Schlaad's compounds have great potential in emerging glycobiology research. I see them having superb opportunities in carbohydrate-based vaccine technologies,' he adds.

Schlaad says that in the future, he hopes to generate smart vesicles with pH- or temperature-responsive membranes. 'External stimuli shall be used to induce either a morphological change or vesicle collapse to trigger cargo molecule or drug release,' he says. *Elizabeth Davies*

## Tea leaves produce cancer-fighting gold nanoparticles

# Time to put the kettle on?

Gold nanoparticles made using chemicals found in tea leaves could be used to combat cancer, say US scientists.

Kattesh Katti, Raghuraman Kannan and colleagues at the University of Missouri, Columbia, used phytochemicals (bioactive compounds) from Darjeeling tea to reduce gold salts to gold nanoparticles. The phytochemicals also stabilised the nanoparticles and covered them in a robust and non-toxic coating. Since only natural chemicals are used in this reaction, no toxic waste products are produced, making it a 100 per cent green process, says Katti.

Tea has been known for its health benefits for centuries and compounds found in tea have been used as dietary supplements and natural pharmaceuticals. The compounds scavenge disease-causing free radicals in the body. They are powerful reducing agents too, but research into these reactions is still in its infancy. Discovering that



phytochemicals in tea can initiate gold nanoparticle formation under non-toxic conditions is of paramount importance for medical and technological applications, says Katti.

**Bioactive compounds in Darjeeling tea produced nanoparticles with anticancer properties**

**Reference**  
S K Nune *et al*, *J. Mater. Chem.*, 2009, DOI: 10.1039/b822015h

Typical reactions for forming gold nanoparticles use toxic chemicals, making them unsuitable as medicines. Also, thiols are used to stabilise and prevent merging of the nanoparticles, but this means that the particles can't bind to drug moieties that target disease sites. Katti's method gets around this problem, as the coating formed by the phytochemicals stops the nanoparticles merging but still allows them to bond with the drug moieties.

Katti's team tested their nanoparticles against prostate and breast cancer cells. They found that the particles had excellent affinity for the cancer cells' receptors, which means that they could be used in anticancer drugs.

'Green nanotechnology is an emerging area interfacing nanotechnology and natural sciences,' says Katti. 'Our process is feasible on larger scales and thus allows the discovery of more medical and technological applications of gold nanoparticles.' *Philippa Ross*

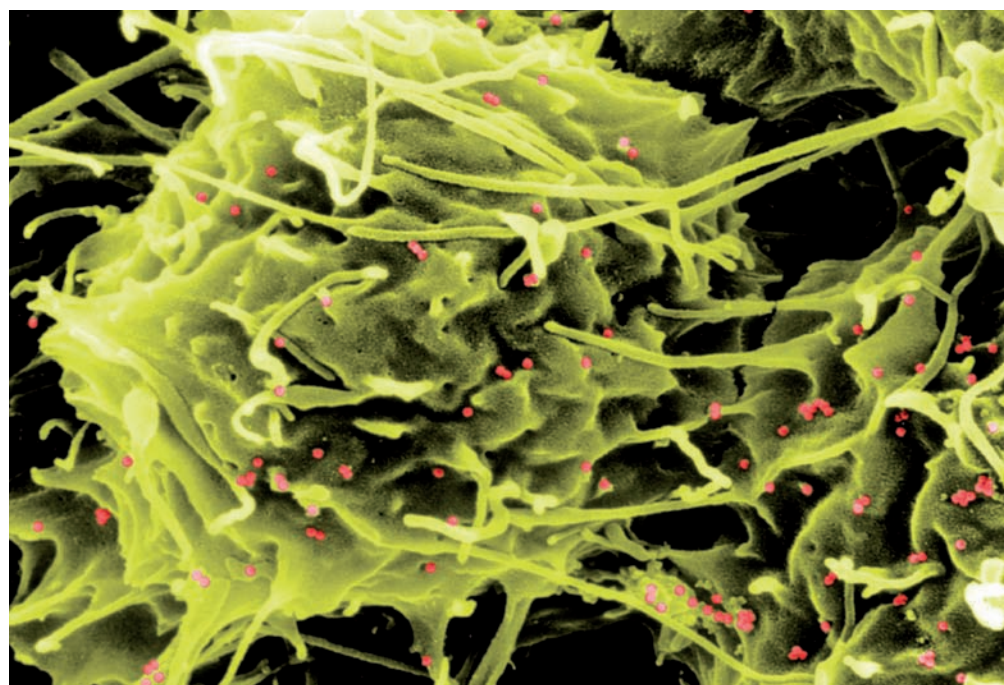
# The growth of nanotoxicology

Christy Haynes and colleagues from the University of Minnesota, US, look at analytical techniques used to assess nanotechnology's effects on health

The use of engineered nanomaterials in consumer products is expanding – a current report by the Woodrow Wilson International Center for Scholars and the Pew Charitable Trusts identifies more than 800 commercial nanomaterial-containing products, accounting for \$147 billion (approximately £104 billion) yearly. The materials show promise in disease treatment or solar power generation. Yet, despite the fact that so many are in commercial use, very little is known about their effects on health. As scientists around the world try to fill this information void, nanotoxicology research has grown rapidly and a wide variety of analytical techniques are used to assess biodistribution (tracking where the compounds travel in the body), cellular uptake and both *in vivo* and *in vitro* toxicity.

Nanotoxicity experiments are typically conducted on mice or rats and focus on LD<sub>50</sub> (exposure amount resulting in 50 per cent population death), changes to tissues or organs, or changes in blood cell populations and serum. These experiments give valuable information but are often time consuming, expensive and provide relatively little mechanistic information about underlying toxicity causes. There is also an ethical imperative to reduce the large animal numbers used in these studies.

*In vitro* assessment may be a better alternative. It can provide inexpensive and rapid nanomaterial interaction analysis on the cellular level. Material uptake and location can be assessed using electron microscopy, fluorescent confocal microscopy or



elemental analysis. On their own, these techniques have limitations so are best used in concert to get a good representation. *In vitro* assessment often relies on using bulk tissue samples from immortalised cell lines and toxicity biomarker probe molecules. *In vivo* toxicity is difficult to predict from the results – some nanomaterial classes (such as carbon nanotubes) interact with probe molecules directly, providing misleading results.

Scientists have developed new nanomaterial distribution and toxicity methods to tackle these challenges, but further methodological developments are needed. These include toxicity analysis techniques to discriminate individual cellular function within

**Toxicology studies reveal nanoparticles' uptake in the body, for example, the iron oxide particles (red) on the surface of white blood cells shown here**

mixed culture environments, label-free dynamic nanoparticle uptake analysis, nanoparticle surface characterisation within complex biological environments and point-of-source nanoparticle exposure analysis for workers.

Also, the worldwide nanotechnology community would benefit greatly from a set of standard toxicity screening protocols for engineered nanomaterials. This would allow scientists to develop safe nanotechnologies and would lessen public fear regarding exposure to nanomaterials, ultimately helping to unlock the full potential of these exciting materials.

Read more in 'Analytical methods to assess nanoparticle toxicity' in issue 3, 2009 of *Analyst*.

**Reference**  
B J Marquis *et al*, *Analyst*, 2009, 425 (DOI: 10.1039/b818082b)

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# Creating a new world

*Mukund Chorghade speaks to Elinor Richards about his fascination with natural products and their role in India's future*



**Mukund Chorghade**

**Mukund Chorghade is President of Chorghade Enterprises and Chief Scientific Officer at THINQ (Technology, Health, Innovation, Novelty and Quality) Pharma, where he provides consultations to pharmaceutical companies on collaborations with academic, government and industrial laboratories. He is also a member of the IUPAC Chemistry and Human Health division.**

## What inspired you to become a chemist?

My father bought me a book called *Chemistry Creates a New World* by Bernard Jaffe when I was a teenager. It opened my eyes to all the wonderful things that chemistry can do. I read it from cover to cover in a day and I was spellbound by a chapter on new pharmaceuticals. I decided that this was what I was going to study, much to the dismay of my father, who wanted me to be a physicist.

## When did your interest in natural products begin?

When I started studying chemistry, a lot of the organic chemistry research was focused on natural products. In India, many professors were working on the isolation of natural products from traditional sources and I was fascinated by the rich variety of structures. We have come full circle because there is now an increased emphasis on the new ideas of reverse pharmacology. This concept brings natural products we have used for centuries back into mainstream sciences and proves the therapeutic efficacy due to their structures.

## What projects are you currently involved in?

At THINQ (Technology, Health, Innovation, Novelty and Quality) Pharma, we define new scalable process routes to new chemical entities. Someone could approach us with a medicinal chemistry route and ask us to make it more efficient, or to find different routes. Our goal is to make the drug better, faster and cheaper. We are also involved in contract medicinal chemistry where we synthesise compounds and analogues; we aim to do the drug discovery work ourselves using collaborations we have established with academics.

## What was your proudest moment?

In my industrial career, I was involved in the discovery of new processes, in particular a route to an antiepileptic drug called Tiagabine, which is now sold as Gabitril. My grandmother had suffered from epilepsy so it gives me a lot of pleasure to see a prescription filled using these particular antiepileptics.

## What is your involvement with IUPAC?

As a member of IUPAC's Chemistry and Human Health division, I have carried out some successful projects. These include compiling new glossaries of terms used in process chemistry and

pharmaceutics and producing a report on the use of natural products in traditional medicines in India and China.

## What is the situation for the pharma industry in India?

Drug discovery as a science is in its infancy, but is a rapidly growing area. Historically, the World Trade Organisation approved deals to allow poorer nations to import generic medicines manufactured in India and China, overriding international patents. Recent changes in the patent laws resulted in increased impetus for Indian pharmaceutical companies to invent new drugs. The government in India has been extraordinarily supportive of such ventures. As yet, there is no Indian drug on the market but I'm very optimistic.

## Do academia and industry collaborate successfully in India?

In India, there can be a gulf between the academic and industrial worlds. Some very good work from industry using state of the art techniques doesn't see the light of day because of patent and confidentiality issues. Another problem is the lack of industrial scientists delivering lectures in symposia. Industry and academia need to be encouraged to collaborate more in order to obtain research funding.

## What is funding like in India?

Now there are increased motivators for doing research in India, the whole scientific infrastructure has increased in size, sophistication and financing. The Indian government has announced many new initiatives where they will fund projects. If you have a good idea and if you can carry out the pioneering research, the government will fund it. Pharma companies in the West have been increasingly looking to India as a font of innovation.

## How do you see the future of chemistry developing?

I'm a tremendous supporter of chemistry, and not just because I am a chemist. I feel that chemistry is still the central science. Sometimes there are new trends and some might say that the computer can solve all your problems, or that biology can solve all the problems. That is not the case. Chemistry, biology and all these other disciplines need to work synergistically with each other.

# Essential elements

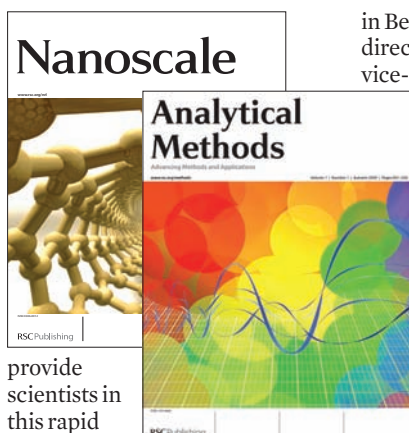
## Announcing two new journals

The prestigious RSC Publishing journal portfolio is set for further expansion with the launch of two new monthly titles in autumn 2009.

*Analytical Methods* will highlight new and improved methods for the practical application of analytical science. The journal will complement the existing RSC journal portfolio of analytical science publications, and with its focus on fundamental and applied modern analytical science, will appeal to both academic and industrial scientists.

*Analytical Methods* was announced at Pittcon in Chicago, IL, US, on 8 March. Delegates had the opportunity to be the first to find out about this exciting new journal.

*Nanoscale* will publish experimental and theoretical work across the breadth of nanoscience and nanotechnology. Highly interdisciplinary, the journal will



provide scientists in this rapid growth field with a new platform characterised by the quality and innovation for which RSC Publishing products are renowned.

*Nanoscale* will be published in collaboration with leading nanoscience research centre, the National Center for Nanoscience and Technology (NCNST)

in Beijing, China. Chunli Bai, director of NCNST and executive vice-president of the Chinese Academy of Sciences, will be editor-in-chief of a new Asia-Pacific editorial office for *Nanoscale*. Markus Niederberger of ETH Zurich, Switzerland, and Francesco Stellacci from Massachusetts Institute of Technology, US, will head two further regional offices in Europe and North America.

From launch, the latest issue of *Analytical Methods* and *Nanoscale* will be freely available to all readers via the website. Free institutional online access to all 2009 and 2010 content will be available following a simple registration process.

Visit [www.rsc.org/methods](http://www.rsc.org/methods) and [www.rsc.org/nanoscale](http://www.rsc.org/nanoscale) to find out more.

## Organic & Biomolecular Chemistry's 150th issue!

Issue 6, 2009 is the 150th issue of *OBC*. Since the first issue was published in January 2003, *OBC* has achieved tremendous success. With an impact factor of 3.167, can any other young journal boast such highly cited papers, published quickly after independent peer review?

Jeffrey Bode, University of Pennsylvania, US, comments, '*OBC* encourages and appreciates the development and application of innovative organic chemistry to a wide variety of contemporary problems. It is our choice for the

publication of new methods and concepts that reach beyond the traditional subdivisions of organic chemistry.'

Take a look at some of the high impact papers from leading scientists published in this 150th issue of *OBC*: a perspective on the design and synthesis of phosphole-based systems for novel organic materials by Yoshihiro Matano and Hiroshi Imahori; an emerging area article on metal-catalysed halogen exchange reactions of aryl halides by Tom Sheppard;

a communication on highly enantioselective asymmetric autocatalysis using chiral ruthenium complex-ion-exchanged synthetic hectorite as a chiral initiator by Kenso Soai and colleagues; and a full paper on ruthenium-based metallacrown complexes for the selective detection of lithium ions in water and in serum by fluorescence spectroscopy by Kay Severin *et al.* Don't miss these and the other articles in this celebratory issue. For more details visit [www.rsc.org/obc](http://www.rsc.org/obc)

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