# ChemComm

Chemical Communications

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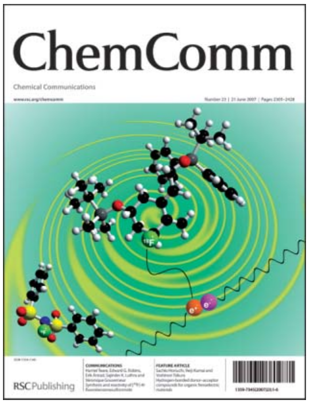
## IN THIS ISSUE

ISSN 1359-7345 CODEN CHCOFS (23) 2305–2428 (2007)



**Cover**

See Sajinder K. Luthra, Véronique Gouverneur *et al.*, *Chem. Commun.*, 2007, 2330.

A new labelling reagent [$^{18}$F]NFSi and two novel radiochemical transformations have been developed for positron emission tomography [PET]. The spiral illustrates the cyclotron necessary for the production of $^{18}$F. The positron emitted from the $^{18}$F-labelled marker annihilates with an electron and generates a gamma pair travelling in opposite directions. Upon detection, this information is used to generate images of activity distribution.

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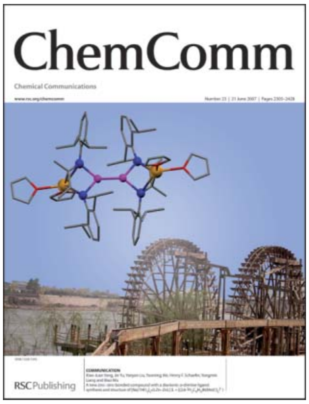


**Inside cover**

See Xiao-Juan Yang, Biao Wu *et al.*, page 2363.

The image shows a zinc–zinc-bonded compound with a dianionic α-diimine ligand, accompanied by a pair of watermills on the Yellow River.

Image reproduced by permission of Xiao-Juan Yang, Jie Yu, Yanyan Liu, Yaoming Xie, Henry F. Schaefer, Yongmin Liang and Biao Wu from *Chem. Commun.*, 2007, 2363.

## CHEMICAL SCIENCE

C41

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

**Chemical Science**

June 2007/Volume 4/Issue 6

www.rsc.org/chemicalscience

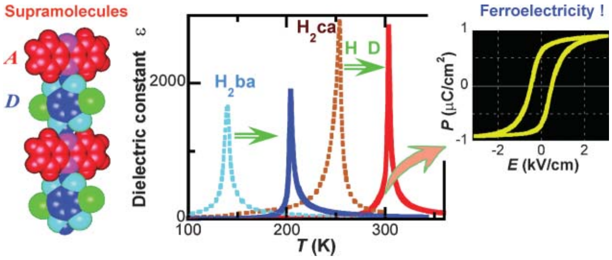
## FEATURE ARTICLE

2321

### Hydrogen-bonded donor–acceptor compounds for organic ferroelectric materials

Sachio Horiuchi,* Reiji Kumai and Yoshinori Tokura

New chemical design strategies towards organic ferroelectric materials are described, highlighting the ferroelectricity and significant dielectric response on a hydrogen-bonded supramolecular assembly of π-conjugated acid and base molecules, in contrast to the conventional use of polar molecules.



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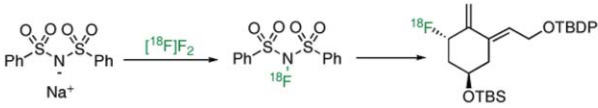
2330

### Synthesis and reactivity of [$^{18}$F]-*N*-fluorobenzenesulfonimide

Harriet Teare, Edward G. Robins, Erik Årstad, Sajinder K. Luthra* and Véronique Gouverneur*

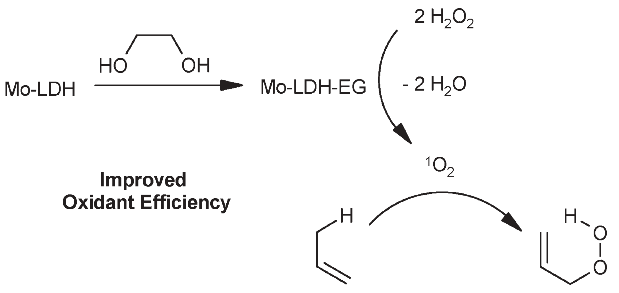


A novel [$^{18}$F]NF reagent and two novel radiochemical transformations have been developed. [$^{18}$F]NFSi has been prepared from sodium dibenzenesulfonimide and reacted in the presence of silyl enol ethers and allylsilanes to deliver labelled fluorinated ketones and allylic fluorides respectively. The radiosynthesis of the fluorinated A ring of vitamin D$_3$ has also been completed with success.

2333

### Glycol-modified molybdate catalysts for efficient singlet oxygen generation from hydrogen peroxide

Joos Wahlen, Dirk De Vos, Walther Jary, Paul Alsters and Pierre Jacobs*

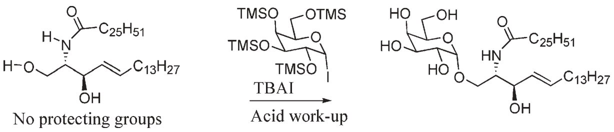


Pretreatment of molybdate-exchanged layered double hydroxides in polyalcohols such as ethylene glycol affords heterogeneous catalysts that generate singlet oxygen from hydrogen peroxide with largely improved oxidant efficiency compared to the unmodified materials.

2336

### Efficient, one-pot syntheses of biologically active α-linked glycolipids

Wenjun Du, Suvarn S. Kulkarni and Jacquelyn Gervay-Hague*

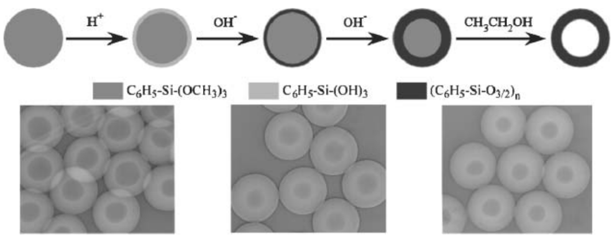


The use of per-*O*-silylated galactosyl iodide provides a transiently protected donor that is highly reactive and capable of undergoing efficient glycosylation with fully functionalized yet unprotected glycolipid acceptors.

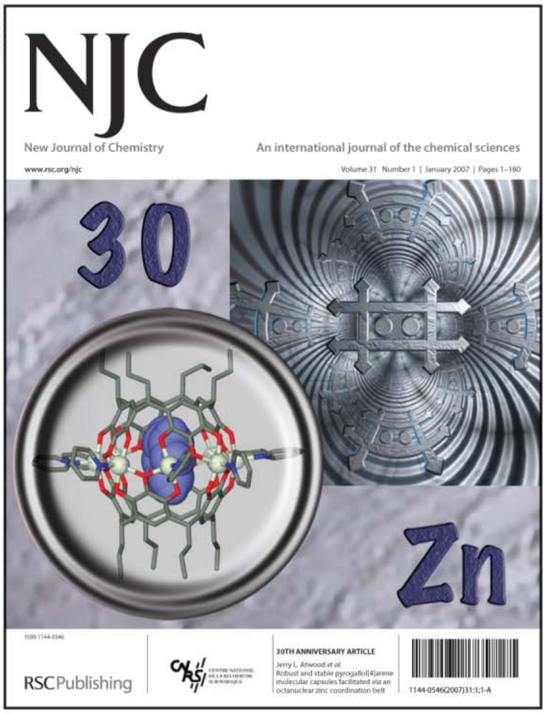
2339

### Mechanism of a self-templating synthesis of monodispersed hollow silica nanospheres with tunable size and shell thickness

Qiangbin Wang,* Yan Liu and Hao Yan*



This study clarifies the mechanism of the hollow structure formation in a simple self-templating preparation of monodispersed hollow silica structures. This new mechanism allowed us to gain better controls for the synthesis of monodispersed hollow structures with tunable sizes and shell thicknesses.

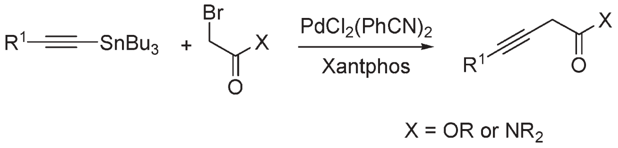

30
Zn

2342

### Alkynylation of α-halocarbonyl compounds—a Stille-type cross-coupling for the formation of C(sp)–C($sp^3$) bonds under neutral conditions

Wei Shi, Chao Liu, Zai Yu and Aiwen Lei*

C(sp)–C($sp^3$) cross-coupling: a direct alkynylation of readily available α-halo esters and amides was explored, and is found to be important and interesting in the syntheses of the 3-alkynoates and 3-alkynoamides in moderate to high yields under neutral conditions.

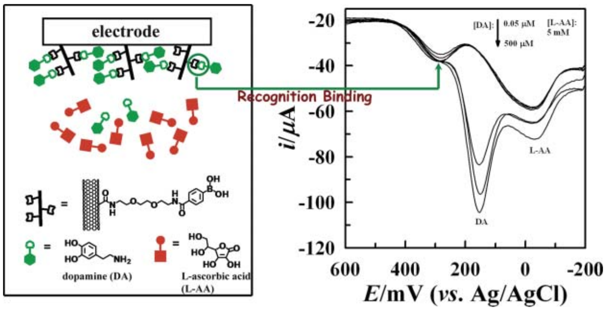


2345

### Sensitive dopamine recognition by boronic acid functionalized multi-walled carbon nanotubes

Wei Wu, Huarui Zhu, Louzhen Fan, Dongfang Liu, Reinhard Renneberg and Shihe Yang*

Boronic acid functionalized multi-walled carbon nanotubes are used for sensitive electrochemical detection of dopamine in the presence of excess L-ascorbic acid *via* specific, reversible formation of a boronate ester.

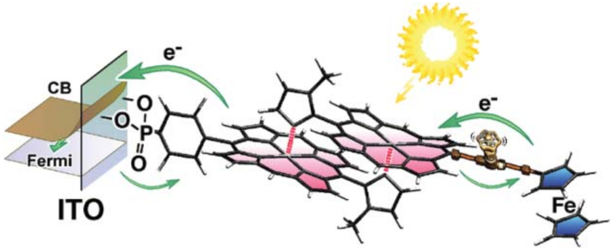


2348

### Fine-tuning of a ferrocene|porphyrin|ITO redox cascade for efficient sequential electron transfer commenced by an $S_2$ photoexcited special-pair mimic

Mitsuhiko Morisue, Dipak Kalita, Noriko Haruta and Yoshiaki Kobuke*

A systematic series of ferrocene/porphyrin redox cascades was assembled through the slipped-cofacial porphyrin dimer on ITO electrode in optimizing the anodic photocurrent generation to perform the highest quantum yield compared to reported values on ITO electrodes.

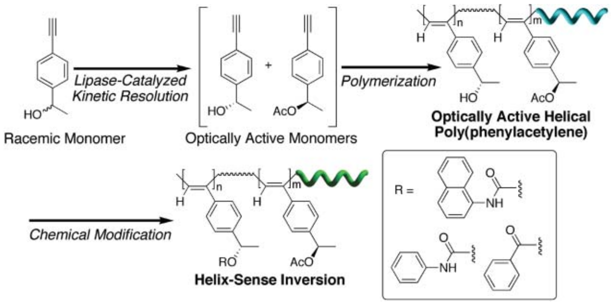


2351

### Macromolecular helicity inversion of an optically active helical poly(phenylacetylene) by chemical modification of the side groups

Shinzo Kobayashi, Kazuhide Morino and Eiji Yashima*

An optically active helical poly(phenylacetylene) was synthesized by the copolymerization of phenylacetylenes bearing optically active hydroxy or ester groups obtained by the kinetic resolution of a racemic phenylacetylene with lipase; the helix-sense inverted from one helix to another by the further chemical modification of the hydroxy groups.



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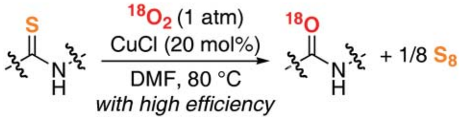
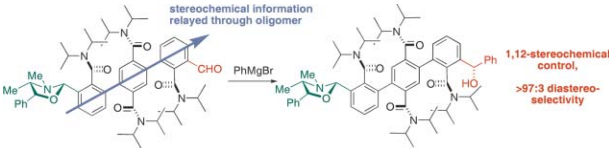


### Copper-catalyzed oxidative desulfurization–oxygenation of thiocarbonyl compounds using molecular oxygen: an efficient method for the preparation of oxygen isotopically labeled carbonyl compounds

Fumitoshi Shibahara,* Aiko Suenami, Atsunori Yoshida and Toshiaki Murai*

A novel copper-catalyzed oxidative desulfurization–oxygenation of thiocarbonyl compounds using molecular oxygen has been developed, and the utility of the process is demonstrated by its application to preparation of a carbonyl-$^{18}$O labeled compounds.

2357

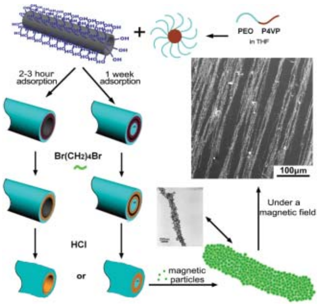


### Transmitting information along oligo-*para*-phenylenes: 1,12-stereochemical control in a terphenyl tetracarboxamide

Jonathan Clayden,* Lluís Vallverdú and Madeleine Helliwell

Conformational interactions between amide substituents mean that a stereogenic centre located at the end of a terphenyl oligomer unit makes its presence felt in remote stereoselective reactions 11 bonds distant.

2360

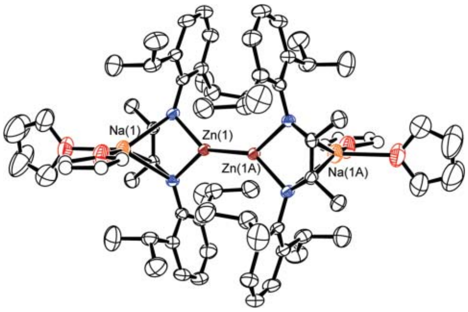


### Facile preparation of stabilized polymeric nanotubes using sacrificial yttrium hydroxide nanotubes as template and block copolymer micelles as precursor

Wenming Shen, Hui Wang, Huisheng Peng, Lei Nie, Daoyong Chen* and Ming Jiang

The facile preparation of stabilized polymeric nanotubes with a hair-like shell is reported using yttrium hydroxide nanotubes as the sacrificial template and block copolymer micelles as the precursor.

2363



### A new zinc–zinc-bonded compound with a dianionic α-diimine ligand: synthesis and structure of $[Na(THF)_2]_2\cdot[LZn–ZnL]$ ($L = [(2,6\text{-}^iPr_2C_6H_3)N(Me)C]_2^{2-}$)

Xiao-Juan Yang,* Jie Yu, Yanyan Liu, Yaoming Xie, Henry F. Schaefer, Yongmin Liang and Biao Wu*

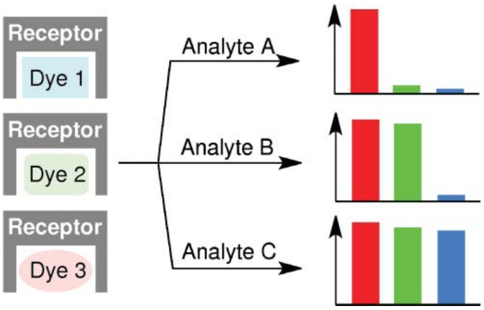
The synthesis and structure of a Zn–Zn-bonded compound supported by a doubly reduced α-diimine ligand, $[Na(THF)_2]_2\cdot[LZn–ZnL]$ ($L = [(2,6\text{-}^iPr_2C_6H_3)N(Me)C]_2^{2-}$) are reported, with a Zn–Zn bond length of 2.399(1) Å.

2366

### Pattern-based sensing of nucleotides in aqueous solution with a multicomponent indicator displacement assay

Andrey Buryak, Alexei Pozdnoukhov and Kay Severin*

A multicomponent indicator displacement assay (MIDA) based on an organometallic receptor and three dyes can be used for the identification and quantification of nucleotides in aqueous solution at neutral pH.

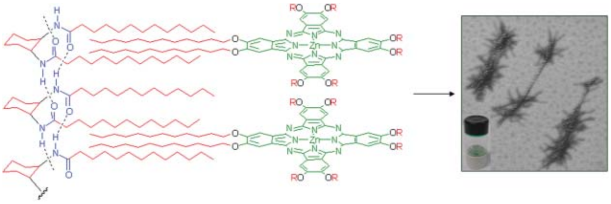


2369

### Physicochemical characterization of octakis(alkyloxy)-substituted Zn(II)-phthalocyanines non-covalently incorporated into an organogel and their remarkable morphological effect on the nanoscale-fibers

David Díaz Díaz,* Tomás Torres,* Rudolf Zentel, Riju Davis and Martin Brehmer

A series of substituted Zn(II)-Pcs were efficiently incorporated into an organogel made of (1*R*,2*R*)-*trans*-1,2-bis(dodecanoylamino)cyclohexane by means of multiple cooperative non-covalent interactions.

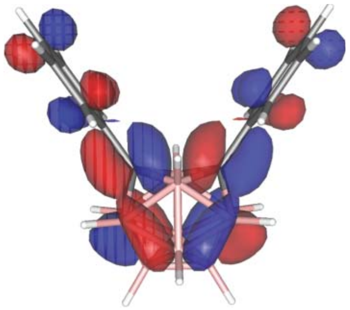


2372

### Carborane radical anions: spectroscopic and electronic properties of a carborane radical anion with a 2*n* + 3 skeletal electron count

Mark A. Fox,* Carlo Nervi, Antonella Crivello and Paul J. Low*

One-electron reduction of 1,2-$Ph_2$-1,2-$C_2B_{10}H_{10}$ (**1**) gives rise to a stable radical anion with a true $2n + 3$ cluster electron count. Excellent agreement is found between the observed spectroscopic features of the radical anion and those calculated from the DFT optimised geometry. There is no significant π-bonding between the cage and the phenyl substituents.

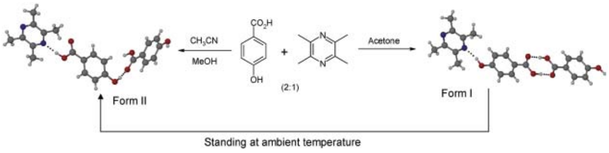


2375

### Supramolecular synthon polymorphism in 2 : 1 co-crystal of 4-hydroxybenzoic acid and 2,3,5,6-tetramethylpyrazine

B. R. Sreekanth, Peddy Vishweshwar* and K. Vyas*

Dimorphic (4-hydroxybenzoic acid)$_2$·(2,3,5,6-tetramethylpyrazine) co-crystal exhibits supramolecular synthon polymorphism. Metastable form I does not follow the hierarchy of hydrogen bonding and converts to stable hierarchic form II.



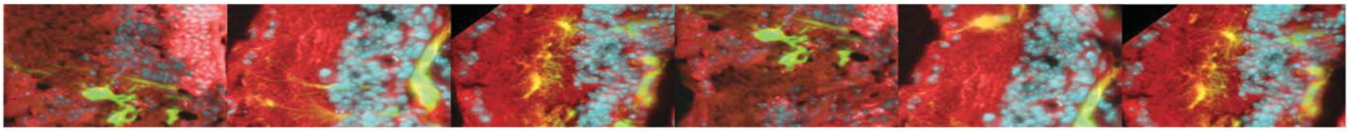
# Tissue Engineering in Microsystems

***Lab on a Chip*** has gathered together a series of articles highlighting the very best research on cell and tissue engineering in microsystems.

**Guest editors** Sangeeta Bhatia (MIT) and Christopher Chen (University of Pennsylvania) have commissioned articles from leading researchers to contribute to this *Lab on a Chip* issue, dedicated to state-of-the-art research on tissue engineering in microsystems.

**The issue includes** a critical review of cell micropatterning techniques; a tutorial review of perfusion culture of mammalian cells; and several high quality full papers on topics covering cell culture, patterning of biomaterials, stem cell differentiation, biocompatible implants, 3D tissue culture, embryoid bodies, cell cytotoxicity analysis and cell-cell communication.

> “Tissue engineering is probably the most promising area of biology and biotechnology, this is an excellent issue featuring the best authors at the leading-edge of on-chip tissue engineering, — congratulations to Chris and Sangeeta”
>
> Andreas Manz, ISAS, Dortmund



**PAPERS INCLUDE:**

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**A chip-based platform for the *in vitro* generation of tissues in three-dimensional organization**
Eric Gottwald, Stefan Giselbrecht, Caroline Augspurger, Brigitte Lahni, Nina Dambrowsky, Roman Truckenmüller, Volker Piotter, Thomas Gietzelt, Oliver Wendt, Wilhelm Pfleging, Alex Welle, Alexandra Rolletschek, Anna M. Wobus and Karl-Friedrich Weibezahn, *Lab Chip* 2007, **7** (6)

**Understanding microchannel culture: parameters involved in soluble factor signaling**
Hongmei Yu, Caroline M. Alexander and David J. Beebe, *Lab Chip* 2007, **7** (6)

**Efficient formation of uniform-sized embryoid bodies using a compartmentalized microchannel device**
Yu-suke Torisawa, Bor-han Chueh, Dongeun Huh, Poornapriya Ramamurthy, Therese M. Roth, Kate F. Barald and Shuichi Takayama, *Lab Chip* 2007, **7** (6)

**Micro-bioreactor array for controllable differentiation of human embryonic stem cells**
Elisa Figallo, Christopher Cannizzaro, Sharon Gerecht, Jason A. Burdick, Robert Langer, Nicola Elvassore and Gordana Vunjak-Novakovic, *Lab Chip* 2007, **7** (6)

**Survival, migration and differentiation of retinal progenitor cells transplanted on micro-machined poly(methylmethacrylate) scaffolds to the subretinal space**
Sarah Tao, Conan Young, Stephen Redenti, Yiqin Zhang, Henry Klassen, Tejal Desai, Michael J. Young, *Lab Chip* 2007, **7** (6)

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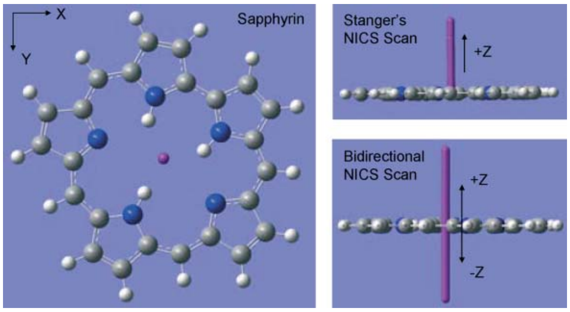
### Evaluation of planarity and aromaticity in sapphyrin and inverted sapphyrin using a bidirectional NICS (Nucleus-Independent Chemical Shift) scan method

Zin Seok Yoon, Su Bum Noh, Dong-Gyu Cho, Jonathan L. Sessler* and Dongho Kim*

Planarity and aromaticity in two structurally related expanded porphyrins were evaluated by two-photon absorption (TPA) measurement and bidirectional NICS scan method.



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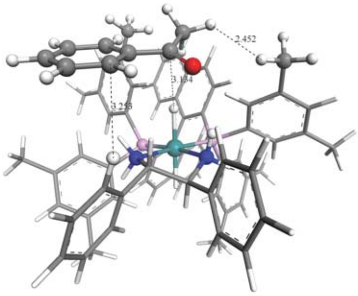
### New insights into the enantioselectivity in the hydrogenation of prochiral ketones

Samuel A. French,* Devis Di Tommaso, Antonio Zanotti-Gerosa, Fred Hancock and C. Richard A. Catlow

The high enantioselectivity in the hydrogenation of acetophenone catalysed by *trans*-Ru(H)$_2$(*S*,*S*-dpen)-(*S*-xylbinap) is explained in terms of the existence of a stable intermediate formed when the reactant enters the catalyst pocket fixing the molecular orientation.

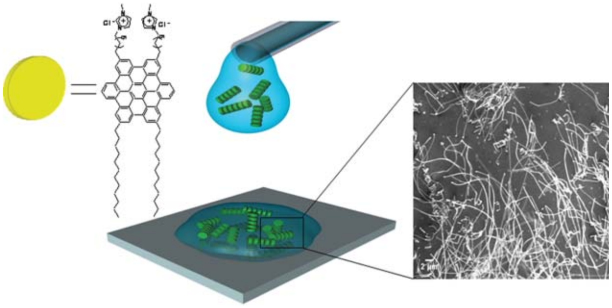


2384

### Self-assembly of amphiphilic imidazolium-based hexa-*peri*-hexabenzo-coronenes into fibreous aggregates

Bassem El Hamaoui, Linjie Zhi, Wojciech Pisula, Ute Kolb, Jishan Wu* and Klaus Müllen*

Imidazolium-based amphiphilic hexa-*peri*-hexabenzocoronenes were synthesized and shown to undergo ordered columnar self-assembly in solid-state as well as in solution to yield defined nanofibers upon solution drop casting onto solid substrate.

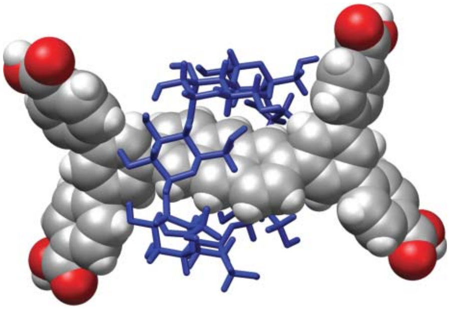


2387

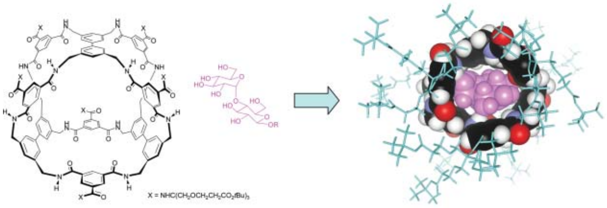
### A cyclodextrin-insulated anthracene rotaxane with enhanced fluorescence and photostability

Matthew T. Stone* and Harry L. Anderson

A β-cyclodextrin anthracene rotaxane was synthesized and found to be significantly more resistant to fluorescence quenching and photobleaching than the uninsulated anthracene derivative.



2390

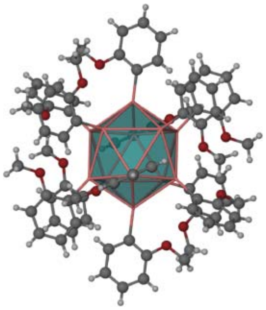


### Selective disaccharide binding by a macrotetracyclic receptor

Emmanuel Klein, Yann Ferrand, Elizabeth K. Auty and Anthony P. Davis*

This new carbohydrate receptor possesses a $C_3$-symmetric polar cavity, large enough to encapsulate disaccharides. Binding to β-maltosyl is preferred, unlike previous systems which have favoured "all-equatorial" substrates.

2393

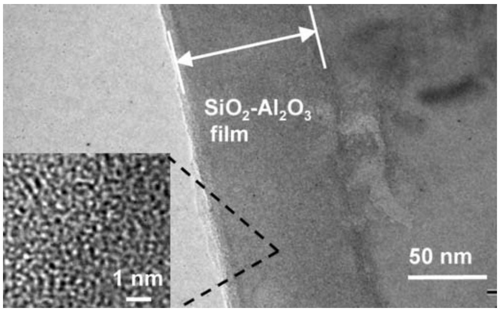


### Icosahedral galloxane clusters

Robert M. McKinlay, Scott J. Dalgarno, Peter J. Nichols, Stavroula Papadopoulos, Jerry L. Atwood* and Colin L. Raston*

Hydrolysis of 'tris(aryl or alkyl)gallium(III)' species affords spheroidal dodecameric galloxane mixed oxide–hydroxide clusters with the gallium centres and residual alkyl/aryl groups arranged at the vertices of pseudo-icosahedra.

2396

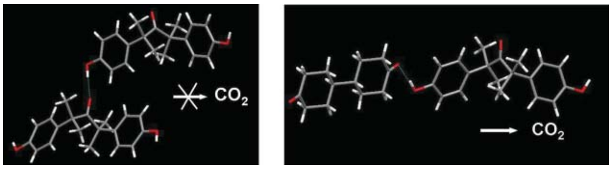


### Efficient proton conduction in dry nanofilms of amorphous aluminosilicate

Yoshitaka Aoki, Emi Muto, Shinya Onoue, Aiko Nakao and Toyoki Kunitake*

Amorphous aluminosilicate nanofilms as prepared by a sol–gel process and post-annealing exhibit proton conduction at a wide temperature range in dry air with a lowest area specific resistance of 0.24 Ω cm$^2$ at 400 °C.

2399



### Hydrogen-bond quenching of photodecarbonylation in the solid state and recovery of reactivity by co-crystallization

Jing Zhang, Milan Gembicky, Marc Messerschmidt and Philip Coppens*

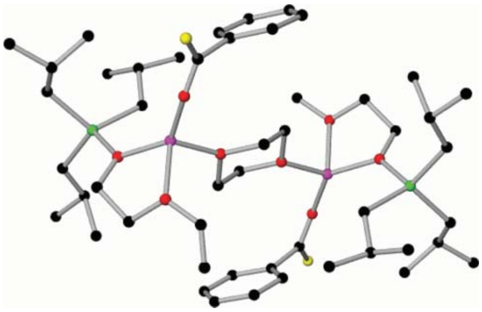
Intermolecular H-bonding between C=O (ketone) and HO (4′-hydroxyphenyl) quenches photodecarbonylation of 2,2,4,4-tetramethyl-1,3-di(4′-hydroxyphenyl)acetone in the crystalline solid state, its reactivity is recovered by co-crystallization with 4,4′ -bicyclohexanone.

2402

### Lewis base stabilized lithium TMP-aluminates: an unexpected fragmentation and capture reaction involving cyclic ether 1,4-dioxane

Joaquín García-Álvarez,* Eva Hevia, Alan R. Kennedy, Jan Klett and Robert E. Mulvey*

A lithium monoamido-trialkyl aluminate that utilises a benzamide as a Lewis base induces the cleavage of dioxane, to release an alkoxy vinyl ether fragment that is trapped by the residue of the mixed-metal base.



2405

### Insertion of arynes into carbon–halogen σ-bonds: regioselective acylation of aromatic rings

Hiroto Yoshida,* Yasuhiro Mimura, Joji Ohshita and Atsutaka Kunai*

Acyl and halogen moieties are introduced simultaneously into adjacent positions of aromatic rings with perfect regioselectivities to give diverse halogenated aryl ketones, which are hardly available by conventional Friedel–Crafts acylation reactions.

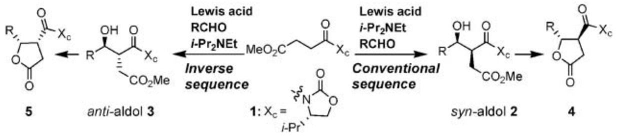
R: aryl, alkenyl, alkyl, alkoxy, carbazoyl
R': alkyl, alkoxy
X: Cl, Br

2408

### Asymmetric aldol reactions under normal and inverse addition modes of the reagents

Saumen Hajra,* Aswini Kumar Giri, Ananta Karmakar and Snehadrinarayan Khatua

Both *syn*- and *anti*-aldol products (**2** and **3**) can be obtained from common reactants (**1**) by simply changing the addition sequence of the base and the aldehyde used. This method also provides a flexible and direct route for the synthesis of *trans*- and *cis*-4,5-disubstituted butyrolactones.

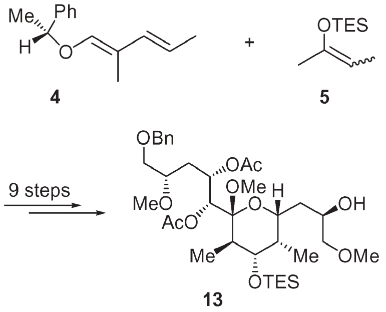


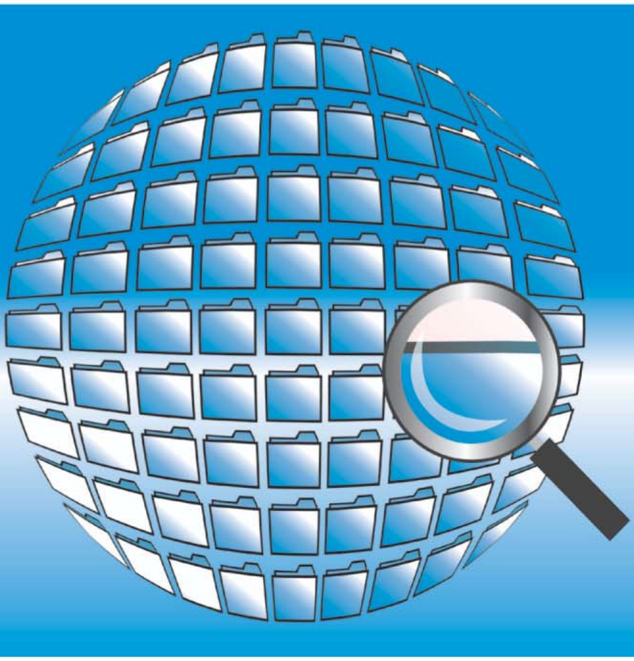
2411

### Short synthesis of the $C_{16}$–$C_{28}$ polyketide fragment of apoptolidin A aglycone

Cotinica Craita, Charles Didier and Pierre Vogel*

New organic chemistry of sulfur dioxide makes quick access to the Koert's $C_{16}$–$C_{28}$ fragment of apoptolidin A aglycone.



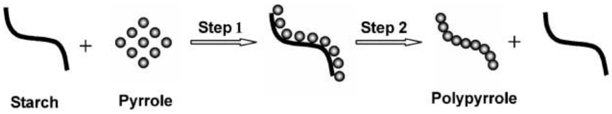


2414

### Starch-assisted synthesis of polypyrrole nanowires by a simple electrochemical approach

Wei Shi, Pengfei Liang, Dongtao Ge,* Jixiao Wang and Qiqing Zhang

Starch, one of the most commonly used polysaccharides, has been adopted for the first time as morphology-directing agent to the electrochemical synthesis of polypyrrole (PPy) nanowires on various electrodes.



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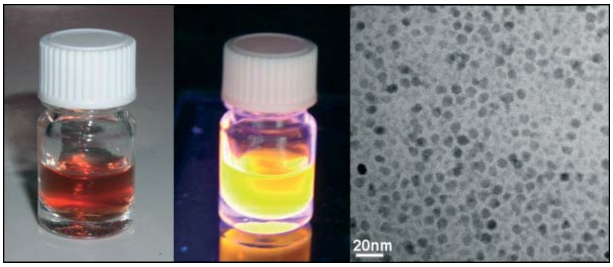
2417

### Amine-induced growth of an $In_2O_3$ shell on colloidal InP nanocrystals

Myriam Protière and Peter Reiss*

In a one-pot reaction colloidal InP nanocrystals are prepared and coated with a 2–3 nm thick $In_2O_3$ shell, increasing their fluorescence efficiency by one order of magnitude.



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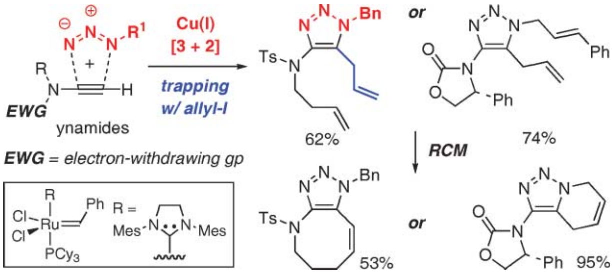
2420

### A triazole-templated ring-closing metathesis for constructing novel fused and bridged triazoles

Xuejun Zhang, Richard P. Hsung* and Hongyan Li

A tandem azide-[3 + 2]-vinyl copper trapping employing ynamides and applications of these triazoles as templates for RCM are described here, combining the two powerful reactions to construct novel triazoles.



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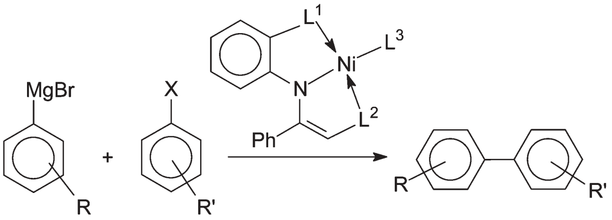
2423

### Amido pincer complex of nickel-catalysed Kumada cross-coupling reactions

Zhong-Xia Wang* and Li Wang

Novel nickel complexes bearing P,N,P-, P,N,N- and N,N,N-amido pincer ligands exhibited highly catalytic activity in Kumada cross-coupling reactions.



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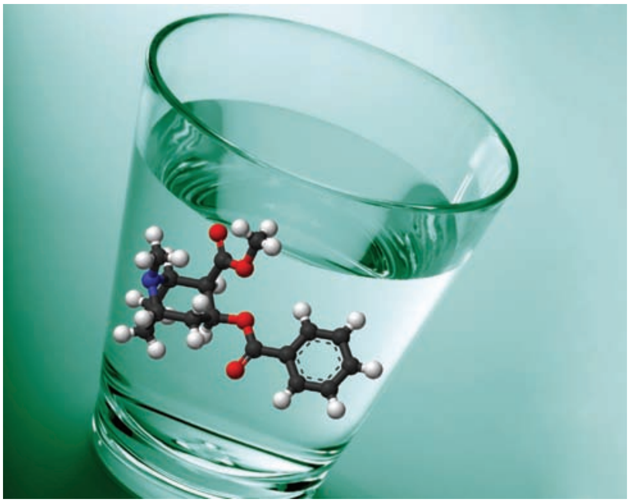
Chemical Science

## Wastewater sampling indicates significant cocaine usage amongst Dubliners

# Something in the water



How much cocaine is going up Dublin's nose? The answer lies in the output from the city's wastewater treatment plants, according to research carried out at Dublin City University by Brett Paull and colleagues. The researchers estimated the levels of consumption of substances such as cocaine and morphine by measuring their concentrations, and the concentrations of their metabolites, in effluent and surface water.[1]

'There are currently very few ways to non-invasively assess community consumption of illicit drugs,' said Paull. 'Social survey data, although useful, is often subject to sampling bias, whereas environmental forensic approaches such as this, when subject to stringent quality assurance and controls, could provide a more accurate assessment.'

Previously, Paull's team surveyed drug contamination on euro banknotes in Dublin.[2] 'However, as an indicator of societal abuse, such samples provide only limited information,' said Paull. But water treatment plants accurately record the volume of water flow and serve a known number of people, allowing total consumption to be estimated.

**Cocaine is just one of the illicit drugs flowing through Dublin's water treatment plants**

Using samples taken from the water plant that serves 1.7 million people within the Dublin metropolitan area, the researchers calculated that more than 220 grams of cocaine flowed through the plant per day. Taking into account the way cocaine is metabolised in the body, this equates to the total consumption of more than 2200 grams of cocaine. The researchers estimate that this is equivalent to a consumption level of about 1.4 grams per 1000 people per day.

'The problem of cocaine consumption is not wholly confined to the capital city,' said Paull. Similar measurements on wastewater treatment plants that serve small towns just outside Dublin revealed consumption levels at about one fifth that of the metropolitan area.

The researchers believe that their method could be used for the routine monitoring of cocaine consumption within a community, revealing any usage trends, such as increases during weekends and public holidays.

*Colin Batchelor*

**References**

1 J Bones, K V Thomas and B Paull, *J. Environ. Monit.*, 2007, DOI: 10.1039/b702799k

2 J Bones, M Macka and B Paull, *Analyst*, 2007, **132**, 208

## In this issue

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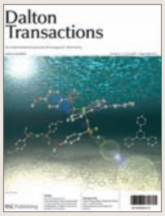
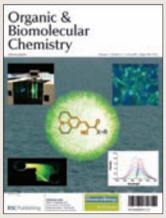
Bill Baker from the University of South Florida, Tampa, US, extols the virtues of cold-water marine natural products

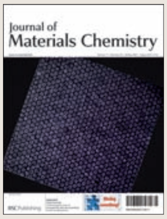


Dalton Transactions



Organic & Biomolecular Chemistry

Lab on a Chip



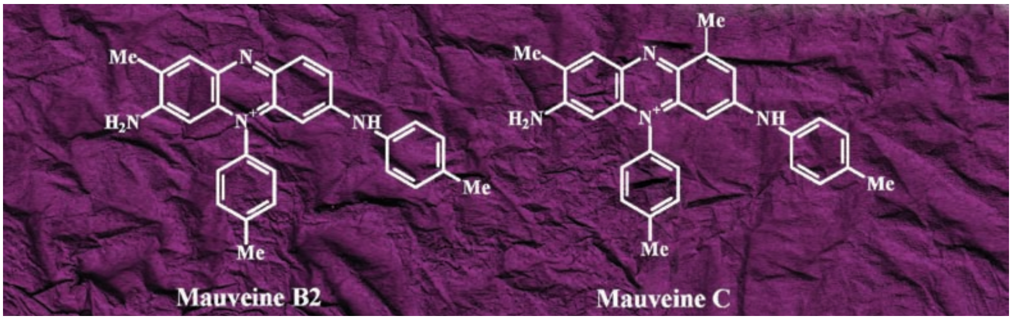
Journal of Materials Chemistry

**A snapshot of the latest developments from across the chemical sciences**

# Research highlights

## Perkin proved right as puzzling purple yields its secrets

## Revealing the mysteries of mauve



Two new compounds have been identified in an original sample of mauveine dye that was made by Sir William Perkin over 150 years ago.

Mauveine, with its characteristic purple colour, was the first synthetic dye molecule, and its production is thought by many to mark the beginning of the modern organic chemical industry. Now, a team of researchers led by João Seixas de Melo at the University of Coimbra and Maria João Melo at the New University of Lisbon, both in Portugal, has discovered two new compounds during its analysis of a historic sample of the dye from the Science Museum in London.[1]

Mauveine dye was already known to contain mauveine A (with two methyl groups) and mauveine B (with three methyl groups).[2] The components discovered by Seixas de Melo and colleagues are mauveine B2, a structural isomer of mauveine B, and a structure with four methyl groups, called mauveine C.

Tony Travis, an expert in the history of chemistry and technology at the Hebrew University of Jerusalem, Israel, welcomed the findings. 'Perkin thought that the commercial mauve dye consisted of more than one component,' said Travis. 'This work shows that even though Perkin was unable to establish the structures of these components, he was correct.'

Using the same starting materials and procedure as Perkin, Seixas de Melo's team made a fresh mauveine sample and compared its composition with that of the historical sample. The different molecular components were separated using high performance liquid chromatography. The chromatograms showed that mauveine B2 and mauveine C were present in both samples.

Seixas de Melo believes the identities of these mauveine constituents have only now been uncovered as a result of the more efficient chromatographic techniques that are available.

'Perkin would be delighted...he spent years trying to establish the constitution and structure of the mauve dye both as a scientific puzzle and because he believed that the constitution would suggest how new derivatives might be made,' said Travis. 'These newly available structures suggest why Perkin failed to prepare a series of derivatives, as had been the case for aniline red.'

Seixas de Melo hopes to extend the study to look at other ancient dyes including indigo and dracoflavylium, a major constituent of the resin known as dragon's blood. *Alison Stoddart*

**Advances in chromatography have allowed previously unknown components of mauveine dye to be revealed**

**Reference**

1 J Sexias de Melo *et al*, *Chem. Commun.*, 2007, DOI: 10.1039/b618926a
2 O Meth-Cohn and M Smith, *J. Chem. Soc., Perkin Trans. 1*, 1994, 5

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## Natural product mimic helps hydrogen chloride to cross membranes

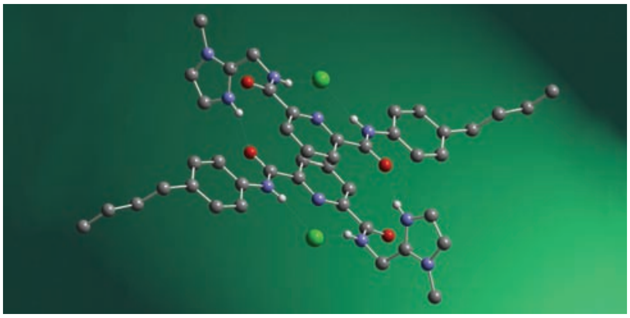
## Double ion carriers offer drug lead

Synthetic molecules that can simultaneously transport two different ions across a membrane could lead to a new class of drugs.

The prodigiosin family of natural products has a variety of therapeutic effects including toxicity to micro-organisms and killing tumour cells. These beneficial activities are linked to the simultaneous transport – known as symport – of hydrogen and chloride ions across a cell membrane. Replicating this co-transport with synthetic molecules opens up the possibility of creating symport based drugs.

Now, a team of researchers led by Phil Gale, at the University of Southampton, UK, and Bradley Smith at the University of Notre Dame, Indiana, US, has managed to do just that. The researchers designed prodigiosin mimics that can efficiently co-transport hydrogen chloride out of vesicles. The team used a pyridine ring modified with two amide groups in the core of the carrier molecule to increase the chloride affinity. The design of the carrier molecule also allowed it to adopt a more organised structure, increasing the efficiency.

'Potentially, this line of research could lead to new therapeutic agents' said Gale. 'The future challenge will be to achieve tissue specificity,' he added. *Russell Johnson*



**Chloride ions (green) fit snugly into the hydrogen bonding pocket of the carrier molecule**

**Reference**

P A Gale *et al*, *Chem. Commun.*, 2007, 1736

## Pores in a cell membrane inspire a new kind of biosensor

# Pores for thought

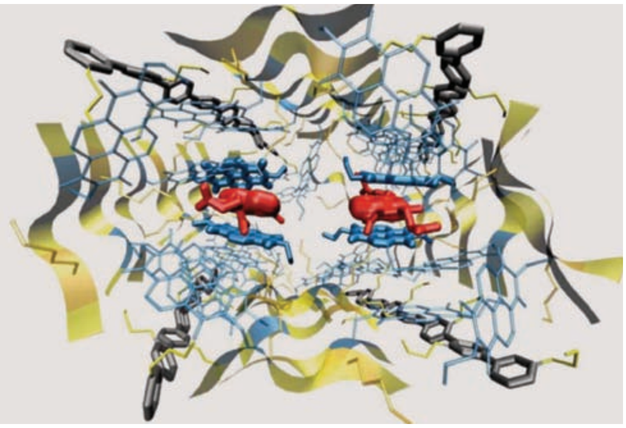
Researchers in Switzerland have made artificial membrane pores that can recognise nucleotides.

Pores in cell membranes are channel-like structures, made from proteins, which allow specific molecules to pass into and out of the cell. These pores can also act as sensors, such as those found in taste receptor cells in the human tongue. Natural sensors like these usually rely on ion-pairing interactions to recognise different molecules.

But the synthetic pore, made by Stefan Matile and colleagues at the University of Geneva, uses a different kind of interaction altogether. Matiles' pore is made from rigid rods functionalised with pentapeptides, which self-assemble into a barrel structure, just like that of a natural pore. The pentapeptides are themselves functionalised with electron-poor naphthalenediimide molecules. A pair of these electron-poor molecules can act as a clamp, sandwiching an electron-rich analyte such as a nucleotide – a subunit of DNA.

'The pores are bioinspired, but it is wonderful to achieve this small victory over nature in utilising this kind of interaction,' said Matile. 'It may even give us access to new analytes.'

Jean-Marie Lehn, an expert in molecular recognition from Louis Pasteur University, Strasbourg, France, said, 'this work will be very important in understanding how natural pores work, and for designing new types of sensor based on this technology.'



**Electron-poor clamps (blue) recognise electron-rich analytes (red)**

**Reference**
H Tanaka *et al*, *Org. Biomol. Chem.*, 2007, **5**, 1369

Matile says there are many potential applications for this kind of system, which could lead to diagnostic sensors for cholesterol, inhibitor screens for drug discovery, or even a synthetic tongue that could 'taste' the difference between sweet, sour and umami. 'The next step is to convince potential investors that this is a viable proposition,' he said.

The synthesis of the pore is not easy, but Matile believes the effort pays off; the high activity of these sensors means that hundreds of thousands of assays can be performed using only milligram quantities of pores. 'Potentially, all that is required in order to realise new applications is the appropriate functionalisation of the pentapeptide with the right type of clamp,' said Matile.

*Stephen Davey*

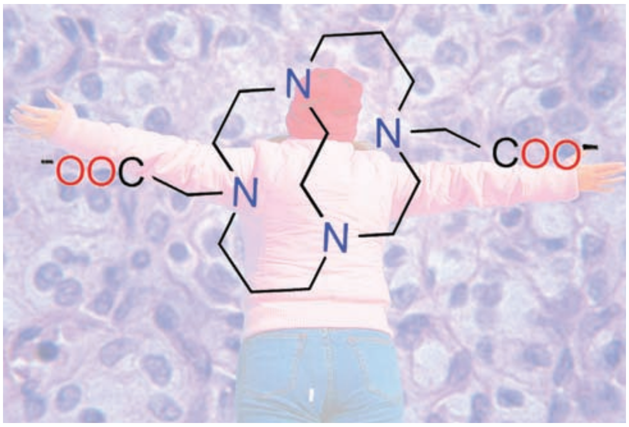
## Radiopharmaceuticals reach their target with shorter arms

# New cancer therapy within reach

Long arms may be useful for reaching the biscuit tin but scientists in the US have shown that shorter arms are better for radiopharmaceuticals.

A team of chemists led by Edward Wong and Gary Weisman at the University of New Hampshire, Durham, and Carolyn Anderson at the Washington University School of Medicine, Missouri, has been investigating molecules that combine with copper to make radiopharmaceuticals. Radioisotopes such as $^{64}$Cu can be used for both the diagnosis and targeted therapy of cancer, but a carrier is needed to get the copper to where it is needed.

Wong's team had previously found a molecule that chelates (or binds to) copper(II) extremely strongly. The molecule consists of a 14-membered ring, known as a macrocycle, that has carboxylic acid groups dangling on pendant arms. Now the scientists have investigated how varying the lengths of the ligand arms of the molecule altered its properties.



**Shorter arms make for a more stable complex**

**Reference**
K J Heroux *et al*, *Dalton Trans.*, 2007, 2150

The results showed that having longer arms made it easier to reduce the copper complex to copper(I), which results in the metal breaking free from the ligand in a process called demetallation. The longer armed molecules also proved to be less stable during in vivo testing.

The researchers plan to work on improving the binding kinetics of the complexes and reducing the harsh conditions currently needed to make the radiopharmaceuticals. They also intend to expand the work to other metals. 'Although radio-copper chelation has been a major goal, we anticipate that other radiometals such as gallium and indium will also form very robust complexes with this family of chelators and expand their application potential,' said Wong.

*Laura Howes*

## News in brief

**Golden glue**
Theoretical chemists predict that gold atoms could serve as a versatile glue to stick molecules together.

**Hydroxy-cruciforms**
Cross-shaped molecules that change colour when exposed to amines could be used to detect compounds used in the manufacture of drugs, pesticides, dyes, preservatives and disinfectants.

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Life could have begun at the poles according to researchers in Germany.

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Polymer scaffolds could one day be used to fix damaged eyes.

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Sugars could be the basis for future HIV vaccines, according to researchers in the US.

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# Nanobombs away!

South Korean scientists have developed a porous silicon nanobomb that heats up with near-infrared irradiation and could cause cancer cells in the body to explode.

Recent research into a new kind of photodynamic therapy has concentrated on using single-walled carbon nanotubes, combined with near-infrared light, to generate heat to kill cancer cells. Now, Chongmu Lee and colleagues from Inha University, Korea, have substituted the carbon nanotubes with a porous silicon nanomaterial, which they claim can generate as much heat as the carbon nanotubes, with the added bonus of producing much smaller amounts of reactive oxygen species.

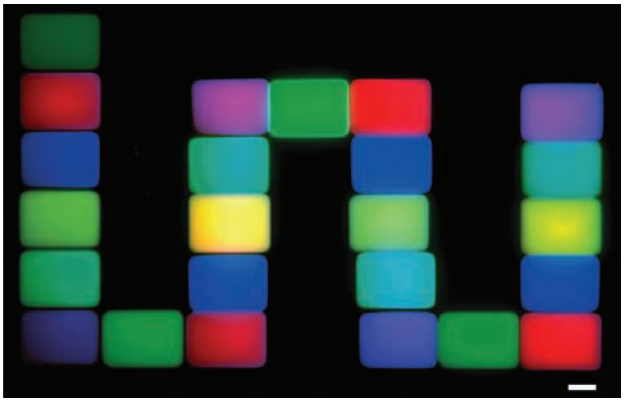
Cancer-killing reactive oxygen species (ROS), generated with traditional photodynamic therapy techniques, can cause a range of side effects in patients undergoing cancer treatment including sensitivity to light, blistered, red or swollen skin if exposed to bright light, feeling or being sick, a metallic taste in the mouth and soreness on swallowing. The ROS accumulated in human bodies might also react with biological molecules to accelerate aging, weaken immunity and eventually cause a number of degenerative diseases.

Lee is hopeful that this work can be developed for cancer treatment, but he admits that there is still a long way to go. 'Although the preliminary results in this work show the feasibility of porous silicon as a new therapeutic agent, it is obvious that much work including teratoma tests and experiments on human bodies is necessary before cancer therapy based on porous silicon is realised,' he said.
*Elinor Richards*

**Porous silicon combined with near-infrared light is a cancer killer**

**Reference**
C Lee *et al*, *J. Mater. Chem.*, 2007, DOI: 10.1039/b700892a

# Fluid approach to 3D microstructures



**Each coloured block represents a different polymer. (Scale bar is 200 micrometers)**

US scientists have developed a cheaper and quicker way of making three-dimensional microstructures.

Samuel Sia's team at Columbia University, New York, used light from a microscope to polymerise specific areas of a fluid inside a microfluidic channel. This process, which causes the fluid to harden and stick to the surface of the channel, is known as photocuring. The unpolymerised material was then washed away and a second material was injected into the channel to be photocured. By repeating this process, Sia built up a three-dimensional microstructure made up of 24 different materials in less than one hour, far quicker than conventional methods.

Sia says that the technique, which combines microscopy with microfluidics, will be useful for studying cell behaviour because the microstructures can mimic complex biological tissues.

Victor Ugaz, an expert in microfluidics at Texas A&M University, College Station, US, welcomes this development. 'This technique allows you to polymerise different materials to create structures with spatial variations in material properties. This may be the most exciting aspect; there is a lot of interest in patterning cells in microenvironments that incorporate these kinds of variations since they may more closely mimic in vivo conditions.'

Sia believes the technique has many potential applications. 'An important next step will be to exploit this capability to make new discoveries, for example in cell-cell communication for the patterning of biocompatible hydrogels,' he said.
*Joanne Thomson*

**Reference**
Y K Cheung *et al*, *Lab Chip*, 2007, **7**, 574

# The crystal ball game

*Is polymorphism crystal clear? Nicola Nugent asks Ashwini Nangia…*

**Ashwini Nangia**

**Ashwini Nangia is a professor of chemistry at the University of Hyderabad, India, and he is a member of the editorial board for *CrystEngComm*. His research interests are focused on crystal engineering and supramolecular chemistry.**

### How did you become interested in chemistry?

Organic chemistry sparked my interest – I had a good teacher at school. Also, I was fascinated with the periodic table – it's a blend of patterns and order on one hand, and then a bundle of exceptions on the other. This combination of method and madness in the same subject is what made me interested in chemistry.

### What kind of research do you do now?

When I first joined the University of Hyderabad, I worked on organic synthesis. About that time, several articles appeared by Dieter Seebach, Fraser Stoddart and George Whitesides. These articles, combined with inspiration from my colleague, Gautam Desiraju, who is a pioneer in crystal engineering, made me look beyond the making of molecules and look at how molecules self-assemble. Since then, my research group has looked at several topics, including host-guest inclusion compounds. We have studied the Cambridge Structural Database to look for recurring patterns and used them in our crystal design approaches. Now, we are focusing on polymorphism and pseudo polymorphism, which is not only an academic challenge, but has great relevance for the pharmaceutical industry.

### Is polymorphism becoming more predictable?

I think we are still very far away from predicting polymorphism. We have a better understanding within families of structures, but not globally. Even the simplest of molecules can be polymorphic, while the most complex structure you can design, based on your logic driven ideas of what should be polymorphic, will turn out to have only a single form. If we start from the basics, a pathway may evolve from which we will understand why certain molecules are polymorphic and how many forms will exist. It goes back to the point I mentioned at the beginning – there is a method, but then there are exceptions, and that's what fuels the curiosity.

### What do you think will be the next big breakthrough in your field?

The major challenges today are: polymorphism, crystal structures with multiple $Z'$ (number of molecules in the asymmetric unit) and crystal structure prediction. We are blending experiment with computation. The blending of these ideas will help us understand what really goes into crystallisation, because it's essentially a one step process – you start with a compound, dissolve it and the next morning, if you are lucky, you get good single crystals. We know the beginning and end of the process, but like any reaction mechanism, we want to know the middle. There have been several recent studies in this area. Hopefully, in the next ten years we'll have a better understanding of what crystallisation really is and how it proceeds.

### What is the secret to running a successful research group?

I think the success of any research group, is down to the students. You can have good ideas, but what drives the idea to reality, at least for experimental chemists, is the student who implements the idea. I have a good group of research students who are able to see the plan or vision that I have when I suggest a problem. Like all research plans, I will be frank enough to admit that many of them don't see reality, but the students are able to get the sense that if one thing doesn't work, something else has to be tried.

### What is the most rewarding aspect of your work?

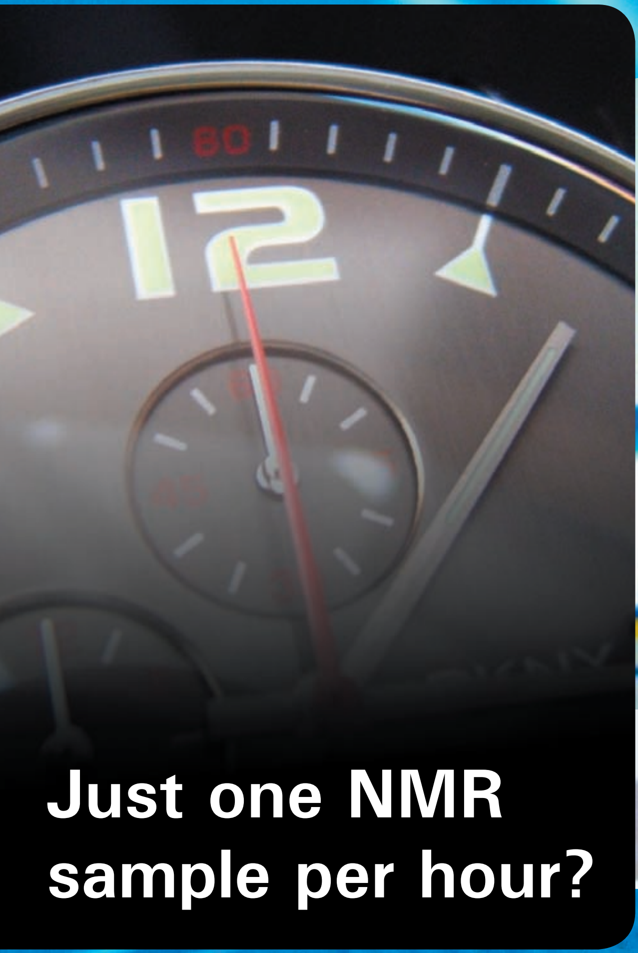
It has always been my dream to work in a contemporary area of research. Being realistic about the facilities in my department, it's pleasing that we are able to do something close to where the latest developments in crystal engineering are happening. I may have been able to do a different type of chemistry, perhaps more instrument based chemistry, if I was working overseas, but it makes me very happy to do the research and produce our results in India.

### What challenges face researchers in India?

The main challenge is attitude. The school system puts emphasis on achieving good grades rather than encouraging innovative thinking and risk taking. The students are wedded to the fact that whatever they do should work, and the first setback they face in research is that most things don't work. But a negative result is not always a bad thing in science. One negative result today may lead to a positive result tomorrow. A shift in thinking is really the biggest challenge.

### What advice would you give to a young scientist?

For any scientist at any point in their life, the most important thing is to do something innovative and challenging. And most of all, whatever you do, you should enjoy it.



## Instant insight

# In from the cold

Bill Baker from the University of South Florida, Tampa, US, extols the virtues of cold-water marine natural products

The words coral and sponge might conjure up pleasant thoughts of warm tropical waters and colourful fishes. The organic chemists among us may think of terpenes and polyketides, while pharmacologists might reflect on anti-inflammatory or anti-cancer agents. That these disparate images are not incongruous is testament to the growing role of marine organisms as sources of biomedically important chemical diversity. Yet much remains to be discovered. With more than 70 per cent of the earth covered by oceans, marine natural products represent only 10 per cent of natural products described to date.

Now modify that word association with the adjectives Antarctic, Arctic, or deep sea. Thoughts of tropical islands flee, along with them chemical or biomedical connotations. Icebergs, abyssal depths and sea water hovering within a few degrees of zero seem at first incompatible with corals and sponges, terpenes and polyketides, and the treatment of human disease. And perhaps for good reason, as these extreme cold regions have traditionally been thought to be lacking in animal life and the accompanying ecological pressure to drive the evolution of chemical defenses. Additionally, the cold-water diving, lack of diving support services and sheer remoteness of many of these habitats renders them difficult to rationalize as practical sources of biological or chemical diversity.

Nonetheless, accumulating biological and chemical research points to a rich cold-water flora and fauna and an active ecology, as dependant upon chemical defenses as many lower latitude habitats. Among bioactivity-producing organisms, sponge biodiversity in Antarctica is as high as that found at temperate latitudes, and deep sea microbial fauna are among the most diverse known. Recent studies have also shown cold-water invertebrate-associated microbe communities are robust.

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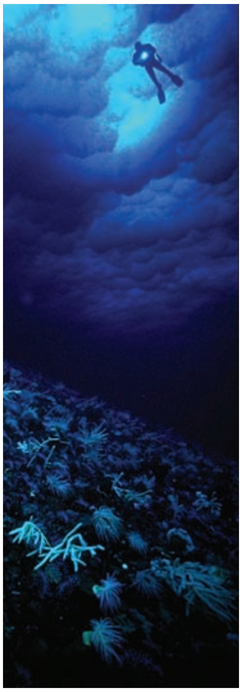
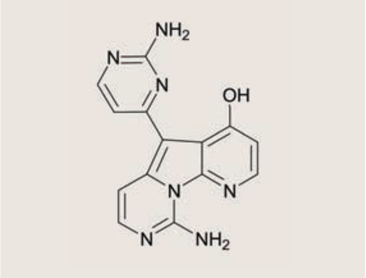


**Diving under ice: not your routine scuba trip**

From the chemical laboratory, unique structural motifs have emerged, as have biological activity profiles that have caught the attention of the pharmaceutical industry. Variolin B, for example, is a structurally unique cyclin-dependent kinase inhibitor from an Antarctic sponge, which is in clinical development as an anti-cancer drug. Meridianins and palmerolides derive from Antarctic tunicates and have advanced in synthetic and pharmacological studies. Meridianins have similar activity to variolin B, while palmerolide A, a potent inhibitor of the enzyme vacuolar-ATPase, targets melanoma. Cold-water natural products are also known to act as antibiotic, antiviral, antifouling, hemolytic, serotonergic, and ion channel modulating agents, as well as inhibitors for a number of specific enzymes.

Besides the accumulating evidence for the biomedical potential of cold-water natural products, the statistics are also encouraging. If the marine realm is largely understudied as a source of chemical diversity, the cold-water habitats are truly unstudied. Consider that 90 per cent of the biosphere is marine, and that a significant portion of that habitat is found at the extreme low end of liquid water's temperature range, yet only 0.3 per cent of natural products reported to date have been isolated from species originating in these environments.



**Antarctic sponges supply variolin B**

What's not to like about cold-water bioprospecting? To be sure, these studies are difficult. Diving under the ice is not your routine scuba diving operation and deep water habitats can only be sampled by ship-based equipment. In polar regions, it is not unusual to have one to three meters of sea ice between diver and ocean, requiring extraordinary measures to gain access to the water. Thermal gear, while quite satisfactory at keeping the diver warm, often weighs as much as, if not more, than the diver, rendering graceful egress from the water impossible. Deep sea trawls, while less physically demanding than scuba diving, present mountains of fragrant biodiversity that must be sorted, often in difficult sea and weather conditions, and are environmentally damaging. Further, while advances in sampling devices have made some deep sea sediments accessible, the abyss remains very difficult to sample.

So the cold-water chemical diversity story has yet to unfold, but the case is compelling. While sampling will always be more challenging in these environments, there is little doubt that chemical rewards of cold-water biodiversity await the intrepid bioprospector.

*Read Bill Bakers review on 'Cold-water marine natural products' in an upcoming issue of* Natural Product Reports.

**Reference**
M D Lebar, J L Heimbegner and B J Baker, *Nat. Prod. Rep.*, 2007, DOI: 10.1039/b516240h

# Essential elements

## Pioneering RSC work on RSS feeds

First came enhanced HTML in electronic journal articles in the first phase of Project Prospect – now further developments means RSC Publishing has become the first ever publisher to enhance RSS feeds with structured subject and compound information.

Journal RSS feeds from RSC Publishing were the first from a scientific publisher to include the graphical abstract. This latest innovation means that RSS feeds from RSC journals will also display ontology terms and compound details, including the 2D image. Users will be able to see at a glance whether the paper is relevant to their research. In addition, hidden coding within the RSS feed allows the metadata to be read by machine – another step towards the 'semantic web'.

This is the latest development in Project Prospect, a unique service developed by RSC Publishing with academic partners. Phase one, launched in February 2007, provided hyperlinked compound information within the HTML, links to terms from the IUPAC Gold Book, plus links from ontology terms to definitions and related papers. Enthusiastically received by authors and readers, feedback since launch has also resulted in improvements to the Toolbox from which these enhancements are available.

Compound structures are now shown with a single click, navigation within the Toolbox has been enhanced – and the Toolbox itself can be made transparent, avoiding any interference in visibility when viewing the article.

To see for yourself, look out for the Project Prospect icon in RSC journal contents lists that identifies enhanced articles. So far, 500 articles have been published that feature these enhancements.

*Find out more at: www.projectprospect.org*

## Article breaks new ground

Research from across four institutions, in two countries, and involving eight researchers published in *Molecular BioSystems* has become the first RSC Open Science paper. Authors from the UK and US collaborated on the work, which involved screening chemical compounds and monitoring changes in tissue during early skeletal development in zebrafish.

The study is an excellent example of research carried out at the chemistry–biology interface, which is a prime focus of the *Molecular BioSystems* journal.

Zebrafish embryos can be monitored relatively easily outside of the uterus and are transparent, so changes can be clearly observed. They serve as models in the study of Menkes disease in humans, a developmental disease associated with copper metabolism.

In the study, mercaptopyridine-*N*-oxide (MCP) was found to affect the development of the notochord, an important tissue involved in early skeletal development. Results suggested that MCP targets the copper-dependent enzyme lysine oxidase.

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## Books on chemistry in industry

The RSC is continually aiming to provide both scientists in the lab and those working in industry with reliable and high-quality reference material. Three recently published titles focus on industry-related topics and make excellent reading:

*Concepts of Chemical Engineering 4 Chemists* (S Simons) – An essential handbook and resource guide for scientists who find themselves working in a chemical engineering-type environment.

*Metal-Catalysis in Industrial Organic Processes* (G P Chiusoli, P Maitlis) – Covers the major areas of the field, discussing the logic of using catalysis in industrial processes as well as the mechanisms involved.


ISTOCKPHOTOS

*Freeze-Drying of Pharmaceuticals and Biopharmaceuticals* (F Franks) – Describes the technology with particular emphasis on the properties of the material to be processed.
*For more information see: www.rsc.org/books*

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