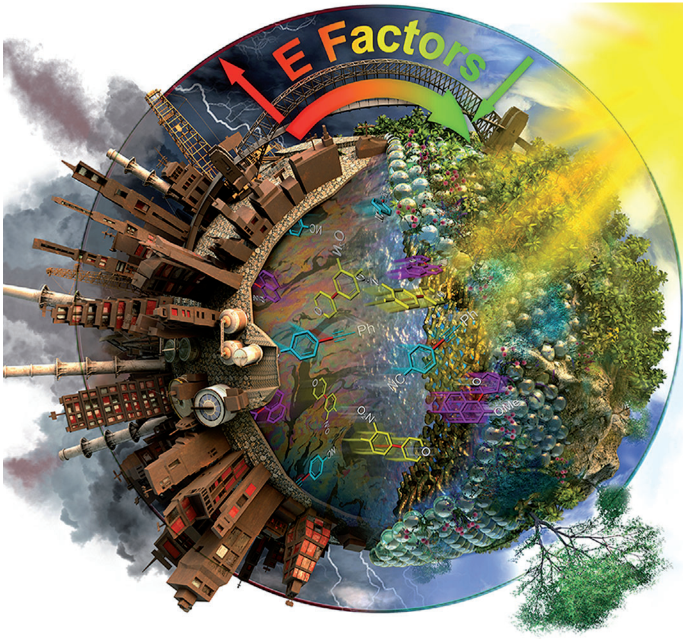
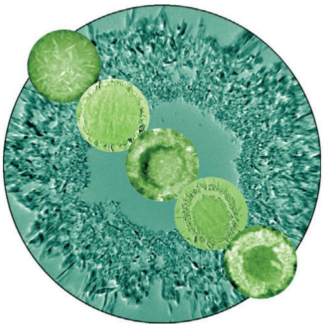
As E Factors drop ...

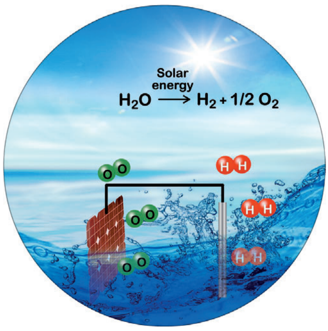


... it's a win-win for chemistry and the environment. In their Minireview on page 10952 ff., B. H. Lipshutz and co-workers document, by direct comparisons with transition-metal-catalyzed cross-coupling reactions from pharma, just how low they can go using a commercially available designer surfactant in water as the reaction medium. As the organic solvent usage drops, E Factors can plummet by as much as an order of magnitude. Let's get organic solvents out of organic reactions, and increase sustainability.

Mesoporous Materials

The preparation of fluffy core-shell, yolk-shell, and hollow anatase nanostructures by a fluorine-free synthetic method is described by D. H. Chen, R. A. Caruso, and L. Cao in their Communication on page 10986 ff.





Electrochemistry

In their Communication on page 11016 ff., W. Luo, Z. Zou et al. report a Ta_3N_5 photoanode with a high solar photocurrent that was prepared by a thermal oxidation and nitridation method.

Natural Products

S. F. Brady and H.-S. Kang describe in their Communication on page 11063 ff. an anthracycline that is encoded by DNA from soil of the Sonora Desert. The compound is active against multidrug-resistant cancer cells and may offer a new approach to cancer therapy.

How to contact us:

Editorial Office:
E-mail: angewandte@wiley-vch.de
Fax: (+49) 6201–606-331
Telephone: (+49) 6201–606-315

Reprints, E-Prints, Posters, Calendars:
Carmen Leitner
E-mail: chem-reprints@wiley-vch.de
Fax: (+49) 6201–606-331
Telephone: (+49) 6201–606-327

Copyright Permission:
Bettina Loycke
E-mail: rights-and-licences@wiley-vch.de
Fax: (+49) 6201–606-332
Telephone: (+49) 6201–606-280

Online Open:
Margitta Schmitt, Carmen Leitner
E-mail: angewandte@wiley-vch.de
Fax: (+49) 6201–606-331
Telephone: (+49) 6201–606-315

Subscriptions:
www.wileycustomerhelp.com
Fax: (+49) 6201–606-184
Telephone: 0800 1800536 (Germany only)
+44(0) 1865476721 (all other countries)

Advertising:
Marion Schulz
E-mail: mschulz@wiley-vch.de
jspiess@wiley-vch.de
Fax: (+49) 6201–606-550
Telephone: (+49) 6201–606-565

Courier Services:
Boschstrasse 12, 69469 Weinheim

Regular Mail:
Postfach 101161, 69451 Weinheim

Angewandte Chemie International Edition is a journal of the Gesellschaft Deutscher Chemiker (GDCh), the largest chemistry-related scientific society in continental Europe. Information on the various activities and services of the GDCh, for example, cheaper subscription to *Angewandte Chemie International Edition*, as well as applications for membership can be found at **www.gdch.de** or can be requested from GDCh, Postfach 900440, D-60444 Frankfurt am Main, Germany.

GDCh
GESELLSCHAFT
DEUTSCHER CHEMIKER

© 2013 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

Get the Angewandte App
International Edition

Available on the App Store

Enjoy Easy Browsing and a New Reading Experience on the iPad
- Keep up to date with the latest articles in Early View.
- Download new weekly issues automatically when they are published.
- Read new or favorite articles anytime, anywhere.

Editorial

"… People who can overturn decades or centuries of conventional thinking through a new experiment or insight do not fit comfortably into a neat top-down, rule-based management system; they are also surprisingly resistant to change …"
Read more in the Editorial by Jeremy K. M. Sanders.

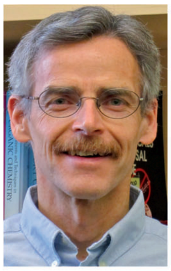
Service

Author Profile

"My greatest achievement has been to combine being a teacher, a researcher, and a popularizer of science for over 50 years.
My worst nightmare is to find myself dumbstruck when I am about to give a lecture …"
This and more about Sir John Meurig Thomas can be found on page 10938.

News


S. A. Snyder


P. Wipf


F. Schüth


D. Milstein


R. Eisenberg

© 2013 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

Books

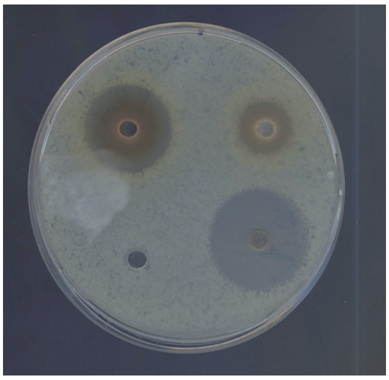
One-Dimensional Nanostructures Tianyou Zhai, Jiannian Yao *reviewed by L. Chi* ______ **10942**

Highlights

Antioxidants

N. Kuhnert* ______ **10946 – 10948**

One Size Does Not Fit All—Bacterial Cell Death by Antibiotics Cannot Be Explained by the Action of Reactive Oxygen Species



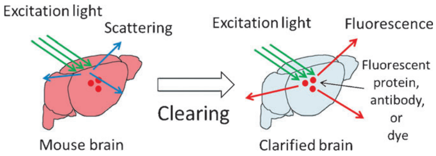
Back to square one: Two recent studies prove that reactive oxygen species (ROS) are not responsible for bacterial cell death after treatment with antibiotics. The ROS concept cannot be generalized to explain all processes resulting in cell death. The search for the mechanism of action of bacterial antibiotics must thus return to the beginning.

Fluorescence Microscopy

D. A. Yushchenko,
C. Schultz* ______ **10949 – 10951**

Tissue Clearing for Optical Anatomy

Quest for transparency: Detailed optical imaging of complex biological entities remains an unmet goal mainly because of the light scattering of biological tissue. A new approach to tissue clearing termed CLARITY is getting us closer to an anatomical view of thick tissues and entire organs with cellular resolution.



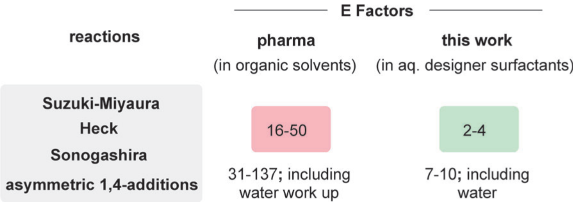
Minireviews

Green Chemistry

B. H. Lipshutz,* N. A. Isley,
J. C. Fennewald,
E. D. Slack ______ **10952 – 10958**

On the Way Towards Greener Transition-Metal-Catalyzed Processes as Quantified by E Factors

Front Cover

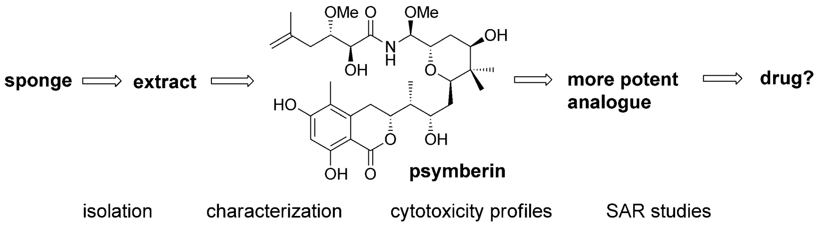


reactions	E Factors pharma (in organic solvents)	 this work (in aq. designer surfactants)
Suzuki-Miyaura Heck Sonogashira asymmetric 1,4-additions	16-50 31-137; including water work up	2-4 7-10; including water

En vogue: Consider greening up palladium-catalyzed reactions by using a minimum amount of water as the only reaction medium, enabled by designer surfactants. Direct comparisons with several commonly used reactions in the pharmaceutical industry illustrate the potential to reduce the dependence on organic solvents, and thereby drive organic waste and, hence, E Factors down and economic benefits up.

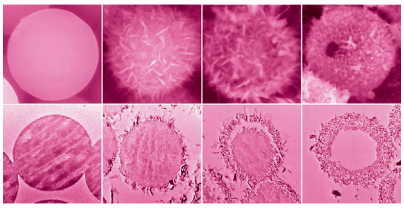
For the USA and Canada: ANGEWANDTE CHEMIE International Edition (ISSN 1433-7851) is published weekly by Wiley-VCH, PO Box 191161, 69451 Weinheim, Germany. Air freight and mailing in the USA by Publications Expediting Inc., 200 Meacham Ave., Elmont, NY 11003. Periodicals postage paid at Jamaica, NY 11431. US POSTMASTER: send address changes to *Angewandte Chemie*, Journal Customer Services, John Wiley & Sons Inc., 350 Main St., Malden, MA 02148-5020. Annual subscription price for institutions: US$ 11.738/10.206 (valid for print and electronic / print or electronic delivery); for individuals who are personal members of a national chemical society prices are available on request. Postage and handling charges included. All prices are subject to local VAT/ sales tax.

Reviews

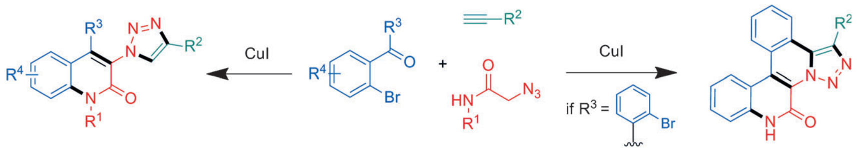


After its isolation from different sponges, the cytotoxic compound psymberin has drawn enormous attention in terms of its structure elucidation and (bio)synthesis because of its fascinating architecture and impressive biological properties. This endeavor resulted in an array of new synthetic strategies that also led to more potent analogues by altering different structural motifs.

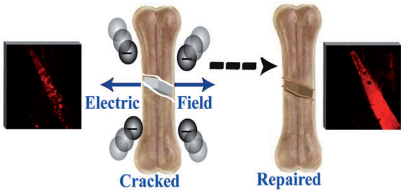
Communications



Versatile synthetic method: Monodisperse anatase microspheres with various complex morphologies have been synthesized by using a versatile fluorine-free solvothermal process in the presence of ammonia. Unambiguous evidence related to surface seeding and a subsequent hollowing process revealed an Ostwald ripening evolution process.

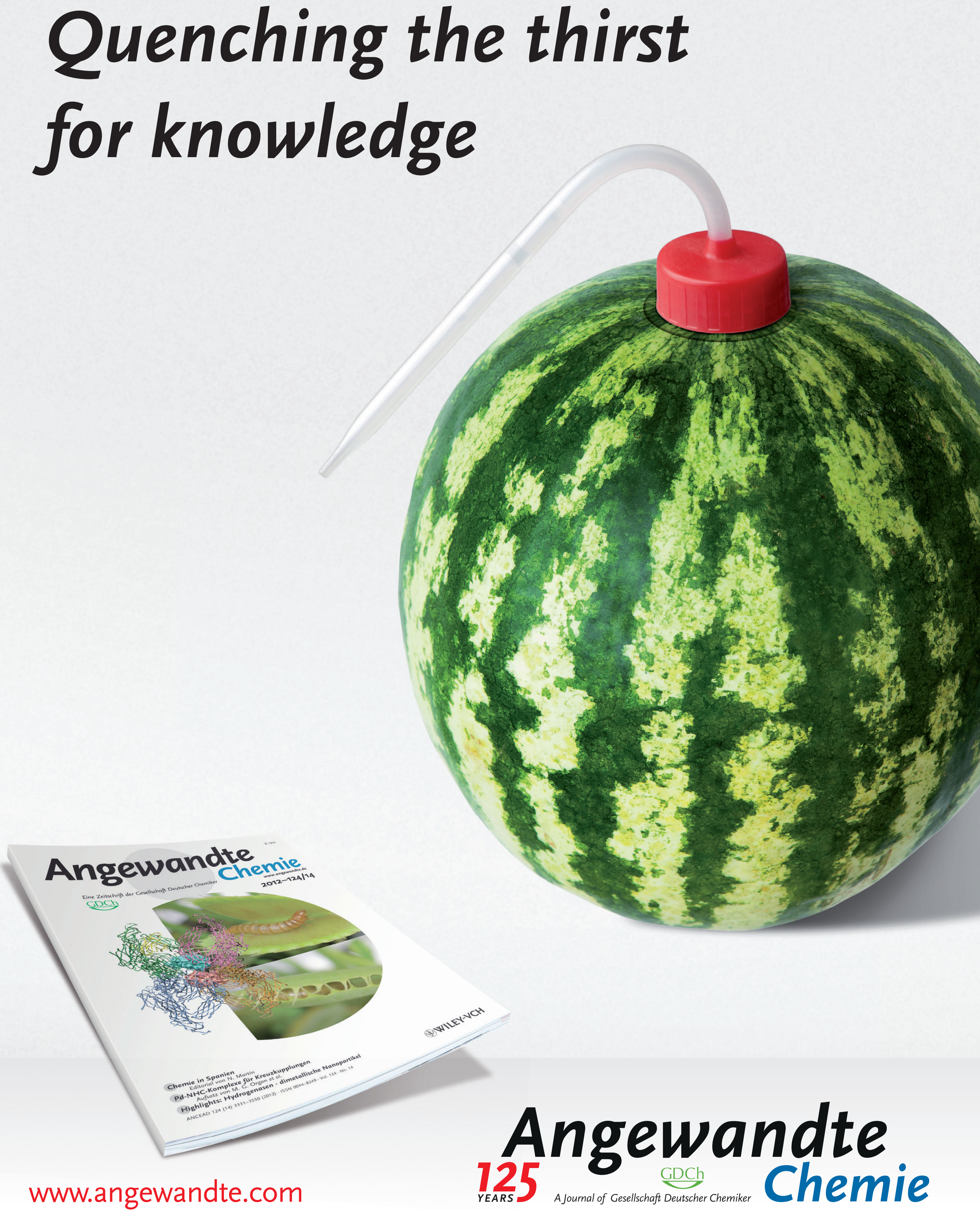


A cat of all trades: A single copper catalyst promoted up to three reaction steps with separate catalytic cycles in a domino sequence (azide–alkyne cycloaddition/Goldberg amidation/Camps cyclization/(C–H arylation)) for the rapid construction of complex heterocycles from three simple components under mild conditions (see scheme). Facile cleavage of the triazole ring enables further elaboration of the condensation products.



Bone cracks can be detected by utilizing the damaged matrix itself as both the trigger and the fuel. A crack in a material with a high mineral content such as bone generates ion gradients, which can be utilized for active targeting and treatment. This approach to targeting a biological structure augments current methods, which are focused on biomacromolecular interactions involving proteins and nucleic acids.

© 2013 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim


Quenching the thirst for knowledge
D 1331
Angewandte Chemie
www.angewandte.de
2012–124/14
Eine Zeitschrift der Gesellschaft Deutscher Chemiker
GDCh
WILEY-VCH
Chemie in Spanien
Editorial von N. Martín
Pd-NHC-Komplexe für Kreuzkupplungen
Aufsatz von M. G. Organ et al.
Highlights: Hydrogenasen · dimetallische Nanopartikel
ANCEAD 124 (14) 3331–3550 (2012) · ISSN 0044-8249 · Vol. 124 · No. 14
www.angewandte.com
Angewandte Chemie
125 YEARS
GDCh
A Journal of Gesellschaft Deutscher Chemiker

The marriage of fire and water: The strongly oxidizing trinitromethyl and strongly reducing BH_3 groups were successfully combined for the first time in the novel $[BH_3C(NO_2)_3]^-$ ion. The stability at room temperature of the new (trinitromethyl)borate is in sharp contrast to the behavior of $[BCl_3C(NO_2)_3]^-$, which already decomposes at −20 °C.

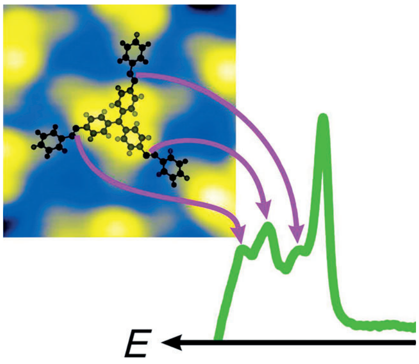
Energetic Materials

G. Bélanger-Chabot, M. Rahm, R. Haiges, K. O. Christe* ———— **11002 – 11006**

$[BH_3C(NO_2)_3]^-$: The First Room-Temperature Stable (Trinitromethyl)borate

---

An asymmetric turn: Scanning tunneling spectroscopy has been used to analyze the structure of tris[4-(phenylazo)phenyl)]amine on a Au(111) surface. A degenerate marker state serves as a sensitive probe for the structure of the adsorbed molecules.

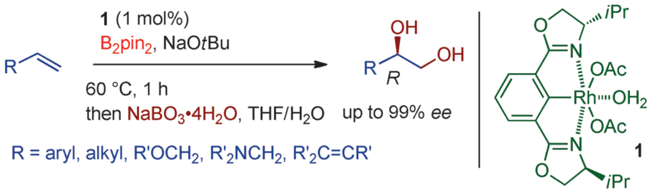


Scanning Tunneling Spectroscopy

T. G. Gopakumar,* T. Davran-Candan, J. Bahrenburg, R. J. Maurer, F. Temps, K. Reuter, R. Berndt ———— **11007 – 11010**

Broken Symmetry of an Adsorbed Molecular Switch Determined by Scanning Tunneling Spectroscopy

---



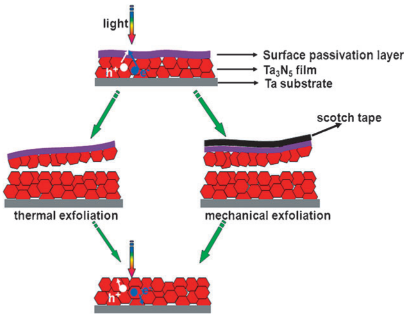
Pin it down: A highly enantioselective diboration of terminal alkenes with chiral **1** and bis(pinacolato)diboron (B_2pin_2) was realized. Subsequent oxidation of the diboron adducts with sodium peroxoborate readily gave the corresponding optically active 1,2-diols in high yields and high enantioselectivities.

Asymmetric Catalysis

K. Toribatake, H. Nishiyama* ———— **11011 – 11015**

Asymmetric Diboration of Terminal Alkenes with a Rhodium Catalyst and Subsequent Oxidation: Enantioselective Synthesis of Optically Active 1,2-Diols

---



Surface exfoliation: A Ta_3N_5 photoanode prepared by a thermal oxidation and nitridation method shows a high solar photocurrent. This photocurrent is currently the highest achieved by a Ta_3N_5 photoanode. The photocurrent is obtained mainly because of facile thermal and mechanical exfoliation of the surface passivation layer of the Ta_3N_5 photoanode (see picture).

Solar Water Splitting

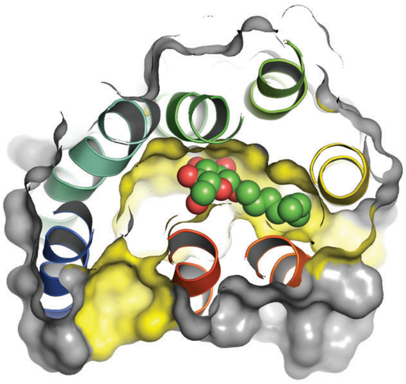
M. Li, W. Luo,* D. Cao, X. Zhao, Z. Li, T. Yu, Z. Zou* ———— **11016 – 11020**

A Co-catalyst-Loaded Ta_3N_5 Photoanode with a High Solar Photocurrent for Water Splitting upon Facile Removal of the Surface Layer

Inside Back Cover

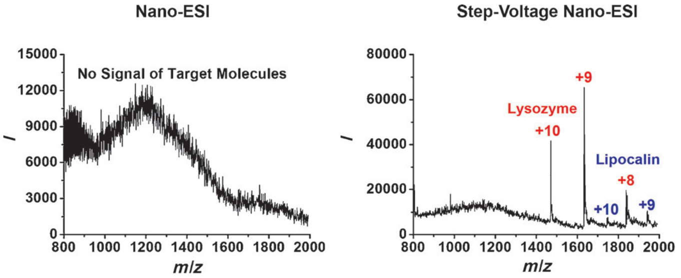
© 2013 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

Structural Biology



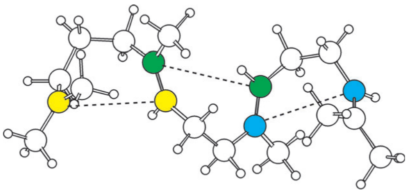
Receptor–ligand interaction: Olfactory receptors (ORs) are G-protein-coupled receptors (GPCRs), which detect signaling molecules such as hormones and odorants. The structure of opsin, the GPCR employed in vision, with a detergent molecule bound deep in its orthosteric ligand-binding pocket provides a template for OR homology modeling, thus enabling investigation of the structural basis of the mechanism of odorant–receptor recognition.

Mass Spectrometry



Matrix unloaded: By changing from fixed-voltage (left) to step-voltage nanoelectrospray (right), the mass-spectrometric analysis of small-volume physiological samples is possible. Separation and ionization are achieved in one process, which avoids sample loss and dilution and prevents interference by the matrix. The result is high sensitivity even for samples at the nanoliter level.

Reaction Mechanisms

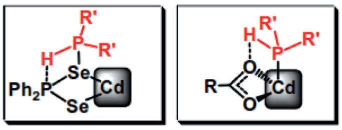


Concerted A–C ring formation: A concerted, but highly asynchronous, pathway was identified for the formation of rings A–C in the biosynthetic conversion of squalene oxide to the prosterol cation, with ring B being formed in the required boat conformation.

Nanocrystal Formation

Two reaction routes of $HPPh_2$

R = $C_{17}H_{33}$ and R' = Ph



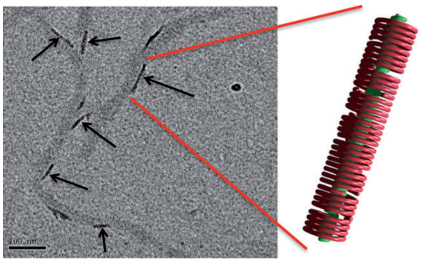
The same P-containing compounds (^{31}P NMR):

$C_{17}H_{33}COO\text{-}PPh_2$	(99 ppm)
$Ph_2P\text{-}PPh_2$	(-14 ppm)
$C_{17}H_{33}COO\text{-}P(Se)Ph_2$	(77 ppm)

One thing in common: The formation of binary colloidal semiconductor nanocrystals from single- ($M(EEPPh_2)_n$) and dual-source precursors (metal carboxylates $M(OOCR)_n$ and phosphine chalcogenides such as $E{=}PHPh_2$) is found to proceed through a common mechanism. For CdSe as a model system ^{31}P NMR spectroscopy and DFT calculations support a reaction mechanism which includes numerous metathesis equilibriums and Se exchange reactions.

© 2013 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

A biomimetic approach has been used for the templated self-assembly of a helical poly(*para*-aryltriazole) foldamer. The solvophobic folding process yields helices that further self-assemble into long nanotubes (see picture; scale bar: 100 nm). Constructs of controlled length and chirality can be generated by applying a poly(γ-benzyl-l-glutamate) scaffold at the appropriate assembly conditions, mimicking tobacco mosaic virus self-assembly.

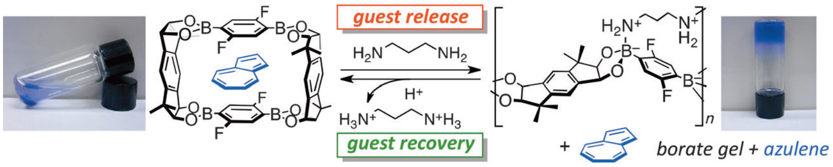


Finite Nanostructures

R. Pfukwa, P. H. J. Kouwer, A. E. Rowan,*
B. Klumperman* ———— **11040 – 11044**

Templated Hierarchical Self-Assembly of Poly(*p*-aryltriazole) Foldamers

---



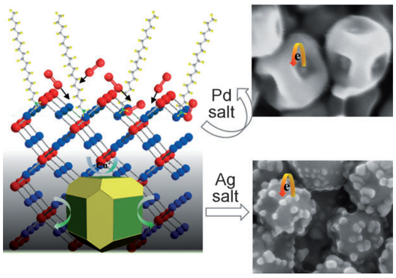
Borate gel formation from guest-encapsulated macrocyclic boronic esters was realized by the addition of a diamine to the suspension of the boronic esters in various organic solvents, which triggered the release of the guest compounds. The guest molecules could be recovered from the borate gel by addition of an acid to remove the diamine, which facilitated the reconstruction of the initial guest-encapsulated macrocyclic boronic esters.

Supramolecular Chemistry

S. Ito, H. Takata, K. Ono,
N. Iwasawa* ———— **11045 – 11048**

Release and Recovery of Guest Molecules during the Reversible Borate Gel Formation of Guest-Included Macrocyclic Boronic Esters

---



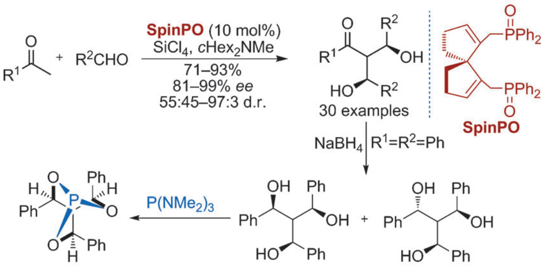
Palladium and silver salts were combined with Cu_2O octadecahedra in concave heterostructures. The formation of concave faces involved selective oxidative etching of Cu_2O on the {100} faces and in situ growth of Pd/Ag on different sites. The structures showed superior catalytic activities to both single domains and their mixtures in a model Sonogashira-type organic reaction.

Concave Hybrid Materials

L. L. Li, X. B. Chen, Y. E. Wu, D. S. Wang,
Q. Peng, G. Zhou,
Y. D. Li* ———— **11049 – 11053**

Pd-Cu_2O and Ag-Cu_2O Hybrid Concave Nanomaterials for an Effective Synergistic Catalyst

---



Symmetry swap: A C_2-chiral spiro diphosphine oxide (SpinPO) has been found to be highly efficient and enantioselective in the catalysis of double-aldol reactions of ketones and aldehydes to give the corresponding optically active double-aldol products, which can be readily transformed into optically active C_3- and pseudo-C_3-symmetric molecules.

Organocatalysis

P. Zhang, Z. Han, Z. Wang,
K. Ding* ———— **11054 – 11058**

Spiro[4,4]-1,6-Nonadiene-Based Diphosphine Oxides in Lewis Base Catalyzed Asymmetric Double-Aldol Reactions

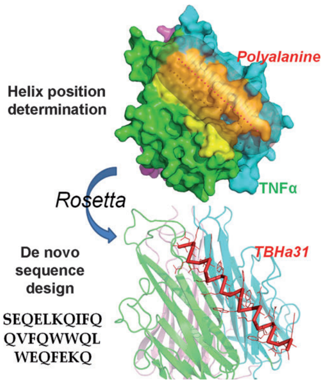
© 2013 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

Protein Design

C. Zhang, Q. Shen, B. Tang, L. Lai* ______ **11059–11062**

Computational Design of Helical Peptides Targeting TNFα

Find and bind: A computational strategy for designing single-helical peptides that can bind to a target protein was developed. After identification of potential helix-binding positions, sequences and binding conformations were derived theoretically, and explored by experimental screening. This method was successfully applied in designing peptide inhibitors for a therapeutic target, tumor necrosis factor-α (TNFα).



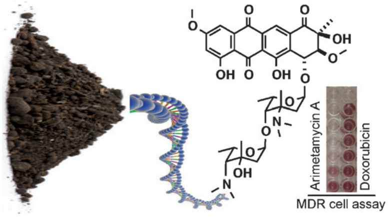
Natural Products

H.-S. Kang, S. F. Brady* _ **11063–11067**

Arimetamycin A: Improving Clinically Relevant Families of Natural Products through Sequence-Guided Screening of Soil Metagenomes

Back Cover

Sequence-tag-guided screening of soil environmental DNA libraries can be used to guide the discovery of new compounds with improved properties. In heterologous expression experiments the eDNA-derived *arm* cluster encodes arimetamycin A (see picture), an anthracycline that is more potent than clinically used natural anthracyclines and retains activity against multidrug-resistant (MDR) cancer cells.

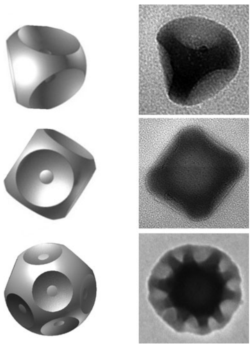


Colloidal Chemistry

A. Désert, C. Hubert, Z. Fu, L. Moulet, J. Majimel, P. Barboteau, A. Thill, M. Lansalot, E. Bourgeat-Lami, E. Duguet, S. Ravaine* ______ **11068–11072**

Synthesis and Site-Specific Functionalization of Tetravalent, Hexavalent, and Dodecavalent Silica Particles

Different shapes: Tetravalent, hexavalent, and dodecavalent silica particles were obtained by the growth of the silica core of binary tetrapods, hexapods, and dodecapods, respectively. The surface of the multivalent particles can be regioselectively functionalized, thereby leading to particles with anisotropic geometry and chemistry.

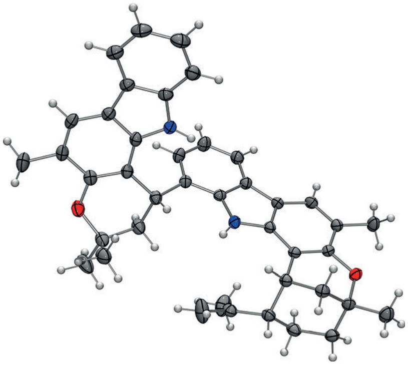


Natural Products

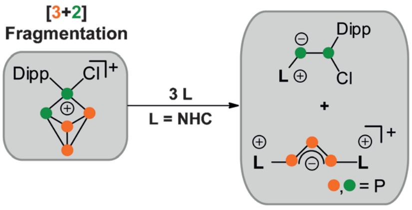
V. P. Kumar, K. K. Gruner, O. Kataeva, H.-J. Knölker* ______ **11073–11077**

Total Synthesis of the Biscarbazole Alkaloids Murrafoline A–D by a Domino Sonogashira Coupling/Claisen Rearrangement/Electrocyclization Reaction

Why take things one step at a time? Aryl–pyran-linked biscarbazole alkaloids of the murrafoline group (see crystal structure of murrafoline A; dark gray: C, red: O, blue: N) were accessed readily by a novel domino reaction sequence involving Sonogashira coupling, a Claisen rearrangement, and electrocyclization. The one-pot procedure enables the straightforward synthesis of these structurally challenging alkaloids in only a few steps.



© 2013 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

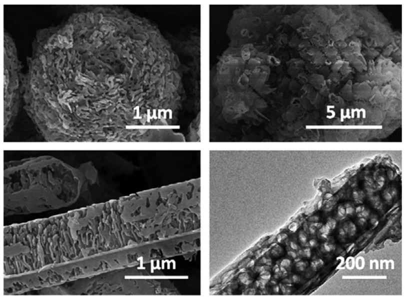


The cage compound [DippP$_5$Cl][GaCl$_4$] (Dipp = 2,6-diisopropylphenyl) reacts with an NHC (N-heterocyclic carbene) by an unprecedented [3+2] fragmentation of the P$_5^+$ core. This yields an imidazoliumyl-substituted P$_3$ species featuring a triphosphaallyl anion motif and a neutral P$_2$ compound. The mechanism of the fragmentation reaction was elucidated by means of experimental and quantum chemical methods.

Phosphorus Compounds

M. H. Holthausen, S. K. Surmiak,
P. Jerabek, G. Frenking,
J. J. Weigand* ———— **11078–11082**

[3+2] Fragmentation of an [RP$_5$Cl]$^+$ Cage Cation Induced by an N-Heterocyclic Carbene

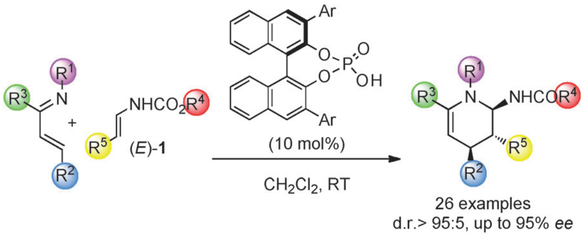


Simple organic cooperative assembly of triazine molecules leads to three-dimensional macroscopic assemblies of low-dimensional graphitic carbon nitrides (g-CNs), for example, nanoparticles, nanotubes, and nanosheets. The approach enables the characterization of the cooperative properties and photocatalytic activities of low-dimensional g-CN materials in hydrogen evolution reactions from water under visible light.

Molecular Cooperative Assembly

Y.-S. Jun, J. Park, S. U. Lee,
A. Thomas, W. H. Hong,
G. D. Stucky* ———— **11083–11087**

Three-Dimensional Macroscopic Assemblies of Low-Dimensional Carbon Nitrides for Enhanced Hydrogen Evolution



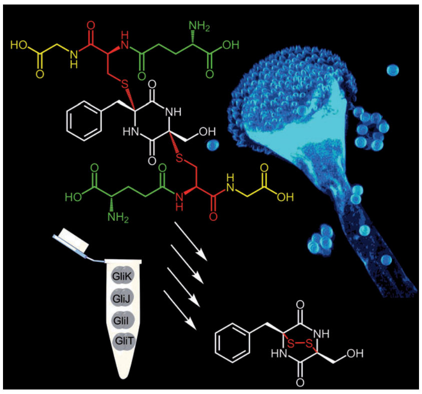
On demand: A highly enantio- and diastereoselective synthesis of 6-amino-trisubstituted tetrahydropyridine compounds has been developed through the inverse-electron-demand aza-Diels–Alder reaction of N-aryl α,β-unsaturated ketimines with enecarbamates (*E*)-**1**. Chiral phosphoric acid catalysts achieve simultaneous activation of both the 1-azadiene and dienophile partners.

Synthetic Methods

L. He, G. Laurent, P. Retailleau, B. Folléas,
J.-L. Brayer, G. Masson* ― **11088–11091**

Highly Enantioselective Aza-Diels–Alder Reaction of 1-Azadienes with Enecarbamates Catalyzed by Chiral Phosphoric Acids

Enzyme quartet: Isolation of the first sulfur-bearing intermediate of the gliotoxin pathway in *Aspergillus fumigatus* and successful in vitro conversion of the bis-glutathione adduct into an intact epidithiodiketopiperazine by a four-enzyme cascade (including glutamyltransferase GliK and dipeptidase GliJ) revealed an outstanding adaptation of a primary metabolic pathway into natural product biosynthesis that is widespread in fungi.



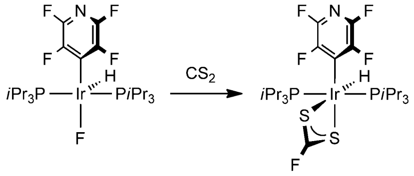
Natural Sulfur Compounds

D. H. Scharf, P. Chankhamjon,
K. Scherlach, T. Heinekamp, K. Willing,
A. A. Brakhage,
C. Hertweck* ———— **11092–11095**

Epidithiodiketopiperazine Biosynthesis: A Four-Enzyme Cascade Converts Glutathione Conjugates into Transannular Disulfide Bridges

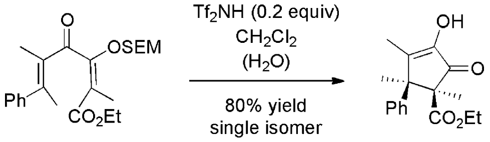
© 2013 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

Reaction Mechanism



CS_2 jumps in: C–F bond formation occurs by reactions of the fluorido complexes *trans*-[Ir(Ar^F)(F)(H)($PiPr_3$)$_2$] (Ar^F = 4-C_5NF_4; see scheme) with CS_2 to form the fluorodithiocarbonato species *trans*-[Ir(Ar^F)(H)(κ^2-(*S*,*S*)-S_2CF)($PiPr_3$)$_2$]. DFT studies suggest an unprecedented concerted metathesis-like mechanism for the C–F bond-formation step in which CS_2 inserts into the Ir–F bond.

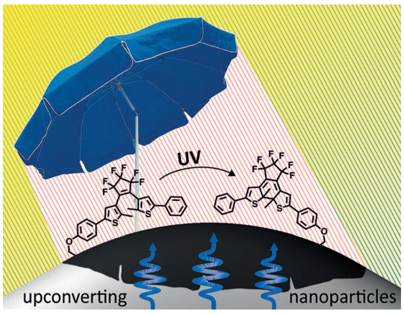
Synthetic Methods



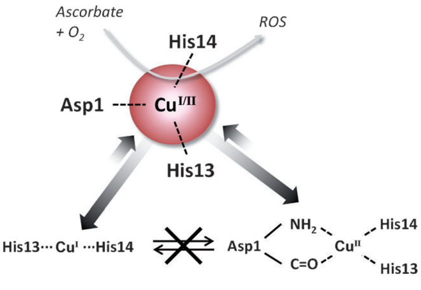
No vacancy: Fully substituted dienones that are highly polarized by a vinylogous carbonate group were found to undergo a remarkably rapid and diastereospecific Nazarov cyclization that led to cyclopentenones with vicinal all-carbon-atom quaternary centers (see example; SEM = 2-(trimethylsilyl)ethoxymethyl, Tf = trifluoromethanesulfonyl).

Photoresponsive Nanoparticles

Sun block for nanoparticles: Unintentional photorelease triggered by UV light is a problem in photodynamic therapy. Encapsulating upconverting nanoparticles containing photoswitches in a UV-blocking amphiphilic polymer shuts down the one-photon process and only allows two-photon-driven photochemistry. Thus, UV light is blocked while NIR light can reach the nanoparticle core and trigger photorelease.



Peptide Oxidation



Copper-amyloid-β ROS production: Copper ions (red sphere, see picture) have been found to accumulate in amyloid-β plaques and play a role in the generation of reactive oxygen species (ROS) within this context. Mass spectrometry studies were able to detail the sites of oxidation damage and shed new light on the mechanism of ROS production, important for the understanding of the pathogenicity of amyloid-β peptides.

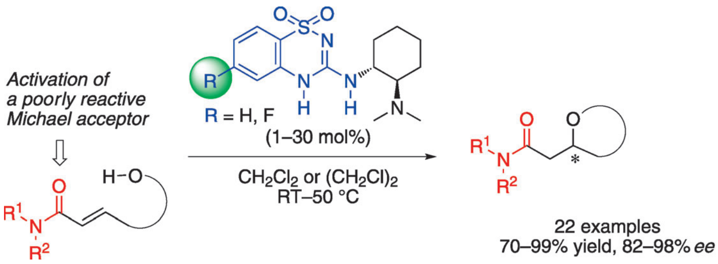
Inside Cover

© 2013 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

Synthetic Methods

Y. Kobayashi, Y. Taniguchi, N. Hayama, T. Inokuma, Y. Takemoto* **11114 – 11118**

A Powerful Hydrogen-Bond-Donating Organocatalyst for the Enantioselective Intramolecular Oxa-Michael Reaction of α,β-Unsaturated Amides and Esters

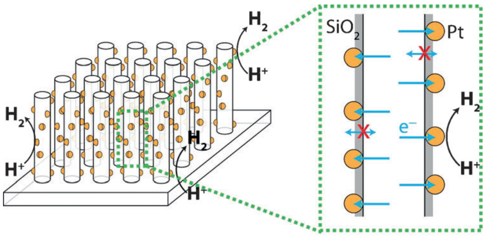


Tuning the organocatalyst: An unprecedented enantioselective intramolecular oxa-Michael reaction of unactivated α,β-unsaturated amides and esters catalyzed by a powerful hydrogen-bond-donating organocatalyst has been developed. Furthermore, the products obtained from this reaction have been used for the straightforward asymmetric synthesis of several natural products and biologically important compounds.

Solar Hydrogen

P. Dai, J. Xie, M. T. Mayer, X. Yang, J. Zhan, D. Wang* ______ **11119 – 11123**

Solar Hydrogen Generation by Silicon Nanowires Modified with Platinum Nanoparticle Catalysts by Atomic Layer Deposition

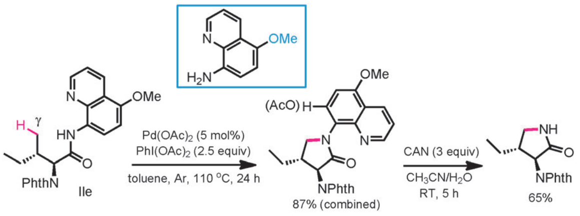


Covered with Pt: A uniform catalyst profile that ensures effective radial charge collection from high-aspect-ratio Si nanowires was achieved by atomic layer deposition of Pt nanoparticles. The resulting photoelectrode permits the measurement of high photovoltages and low overpotentials, and leads to very good stability against photooxidation of Si nanowires in solar water-reduction reactions.

C–H Functionalization

G. He, S.-Y. Zhang, W. A. Nack, Q. Li, G. Chen* ______ **11124 – 11128**

Use of a Readily Removable Auxiliary Group for the Synthesis of Pyrrolidones by the Palladium-Catalyzed Intramolecular Amination of Unactivated γ C(sp^3)–H Bonds



Easy on, easy off: Directing groups found to promote the palladium-catalyzed amination of γ C(sp^3)–H and C(sp^2)–H bonds of secondary amides included 5-methoxy-8-aminoquinoline, which can be removed under mild conditions (see scheme; CAN = ceric ammonium nitrate). In conjunction with a β-C–H methylation or γ-C–H arylation step, the γ-C(sp^3)–H amination provided access to complex pyrrolidones from readily available precursors.

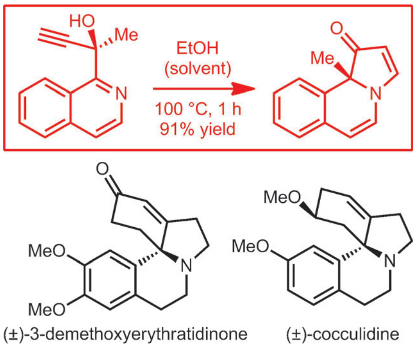
© 2013 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

Alkaloid Synthesis

S. T. Heller, T. Kiho, A. R. H. Narayan,
R. Sarpong* ______ 11129 – 11133

Protic-Solvent-Mediated Cycloisomerization of Quinoline and Isoquinoline Propargylic Alcohols: Syntheses of (±)-3-Demethoxyerythratidinone and (±)-Cocculidine

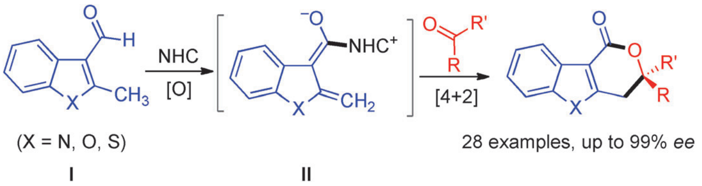
Putting the “benz” in indolizinones: A cycloisomerization approach to benz[*g*]indolizinones and benz[*e*]indolizinones provides the first general route to these unique azacycles (see example). The utility of the benzindolizinone products was demonstrated by the application of this method to the total synthesis of the *Erythrina* alkaloids 3-demethoxyerythratidinone and cocculidine.



Asymmetric Organocatalysis

X. Chen, S. Yang, B.-A. Song,*
Y. R. Chi* ______ 11134 – 11137

Functionalization of Benzylic C(sp^3)–H Bonds of Heteroaryl Aldehydes through N-Heterocyclic Carbene Organocatalysis



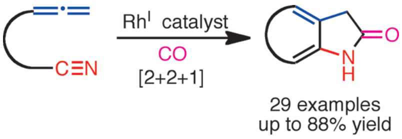
Aryl aldehyde activation: Oxidative activation of 2-methylindole-3-carboxaldehyde (**I**) through N-heterocyclic carbene (NHC) organocatalysis generates heterocyclic *ortho*-quinodimethane (**II**) as a key intermediate. This intermediate then undergoes formal [4+2] cycloaddition with trifluoromethyl ketones or isatins to form polycyclic lactones containing a quaternary carbon center.

Heterocycles

T. Iwata, F. Inagaki,
C. Mukai* ______ 11138 – 11142

Progress in Carbonylative [2+2+1] Cycloaddition: Utilization of a Nitrile Group as the π Component

New tricks, old reactions: The treatment of 2-(1,2-propadienyl)phenylacetonitrile derivatives with a catalytic amount of [{RhCl(CO)dppp}$_2$] (dppp = 1,3-bis(diphenylphosphanyl)propane) under a CO atmosphere produced benzo[*f*]oxyindole derivatives (see scheme). This aza-Pauson–Khand-type reaction was applicable to aliphatic substrates, thus resulting in the formation of the azabicyclo[3.3.0]octadienone derivatives.

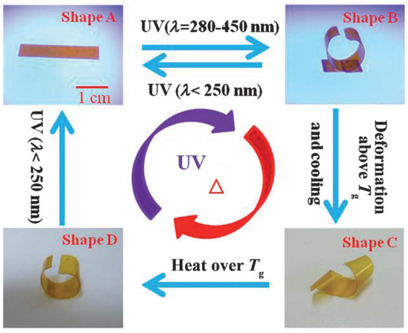


Smart Materials

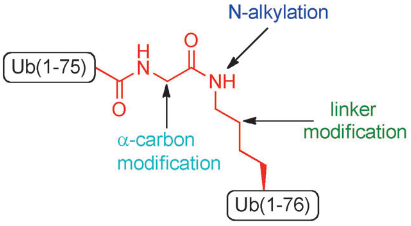
S.-Q. Wang, D. Kaneko, M. Okajima,
K. Yasaki, S. Tateyama,
T. Kaneko* ______ 11143 – 11148

Hyperbranched Polycoumarates with Photofunctional Multiple Shape Memory

In good shape: The films of hyperbranched polycoumarate derivatives can undergo a reversible [2+2] cycloaddition under irradiation of UV light and behave like photomechanical elastomers. From a predetermined original shape A the photonically and thermally memorized shapes B and C were obtained. The original shape was recovered by photoirradiation (see picture; T_g = glass transition temperature).



© 2013 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

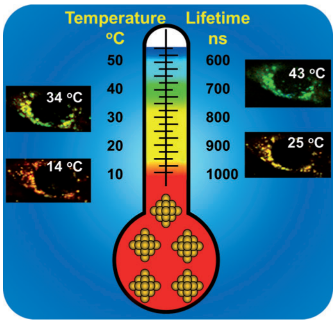


In every direction: Chemical protein synthesis allows the construction of 14 di-ubiquitin analogues modified in the vicinity of the isopeptide bond to examine their behavior with deubiquitinases and ubiquitin binding domains. The results set the ground for the generation of unique probes for studying the interactions of these chains with various ubiquitin-interacting proteins.

Protein Chemistry

N. Haj-Yahya, M. Haj-Yahya,
C. A. Castañeda, L. Spasser,
H. P. Hemantha, M. Jbara, M. Penner,
A. Ciechanover, D. Fushman,
A. Brik* ______ **11149 – 11153**

Modifying the Vicinity of the Isopeptide Bond To Reveal Differential Behavior of Ubiquitin Chains with Interacting Proteins: Organic Chemistry Applied to Synthetic Proteins

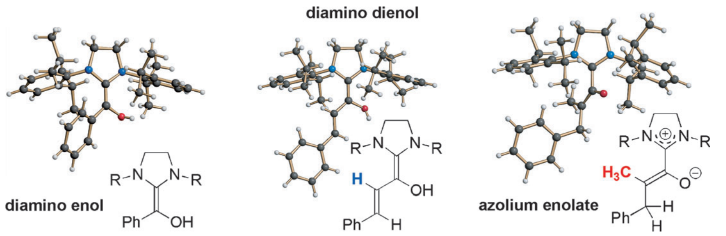


The “gold standard” for nanothermometry: The application of ultrasmall, near-IR-emitting fluorescent gold nanoclusters (AuNCs) for temperature sensing has been explored. AuNC-based fluorescent nanothermometry features excellent thermal sensitivity and simultaneous temperature sensing and imaging in HeLa cells.

Fluorescence Nanothermometers

L. Shang, F. Stockmar, N. Azadfar,
G. U. Nienhaus* ______ **11154 – 11157**

Intracellular Thermometry by Using Fluorescent Gold Nanoclusters

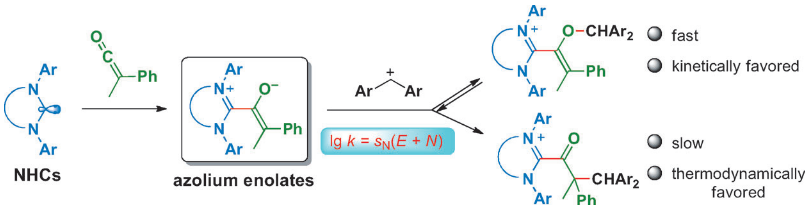


Caught in the act: Diamino enols, diamino dienols, azolium enolates, and azolium enols are postulated intermediates of the N-heterocyclic carbene catalyzed umpolung of aldehydes and enals. Several of these elusive reaction intermediates were generated with the saturated imidazolidin-2-ylidene SIPr (R = 2,6-bis(2-propyl)phenyl) and characterized by NMR spectroscopy and X-ray crystallography.

Organocatalysis

A. Berkessel,* V. R. Yatham, S. Elfert,
J.-M. Neudörfl ______ **11158 – 11162**

Characterization of the Key Intermediates of Carbene-Catalyzed Umpolung by NMR Spectroscopy and X-Ray Diffraction: Breslow Intermediates, Homoenolates, and Azolium Enolates



Oxygen versus carbon: Azolium enolates were generated by the reactions of N-heterocyclic carbenes (NHCs) with methyl phenyl ketene and characterized by X-ray crystallography. Kinetic studies show that the enolate oxygen is 20 times more nucleophilic than the carbon atom, but under thermodynamic control exclusive C-addition products were formed.

Organocatalysis

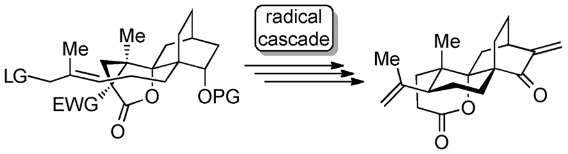
B. Maji,* H. Mayr* ______ **11163 – 11167**

Structures and Ambident Reactivities of Azolium Enolates

Natural Product Synthesis

S. Breitler, E. M. Carreira* **11168 – 11171**

Total Synthesis of (+)-Crotogoudin



(+)-Crotogoudin

Fellowship of the ring: The first total synthesis of (+)-crotogoudin, a 3,4-*seco*-atisane diterpenoid natural product, is reported. Asymmetric access to the bicyclo[2.2.2]octane core is achieved through a desymmetrization of a *meso*-diketone with baker's yeast (LG = leaving group, PG = protecting group). A SmI_2-induced radical cyclopropane-opening/annulation/elimination cascade affords the suitably decorated tetracyclic structure of (+)-crotogoudin. The synthesis led to revision of the reported optical rotation of the natural product and to assignment of its absolute configuration as an *ent*-atisane (5*R*,10*R*).

Supporting information is available on www.angewandte.org (see article for access details).

A video clip is available as Supporting Information on www.angewandte.org (see article for access details).

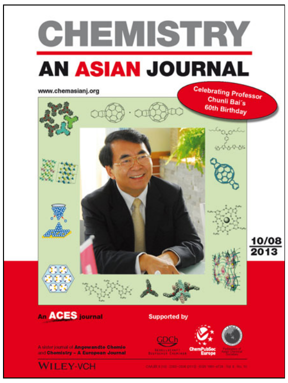
This article is available online free of charge (Open Access).

This article is accompanied by a cover picture (front or back cover, and inside or outside).

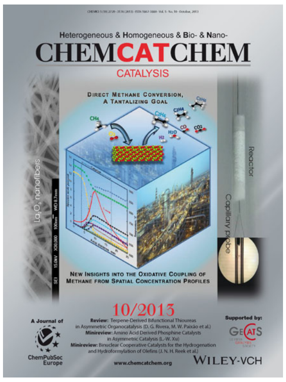
The Very Important Papers, marked VIP, have been rated unanimously as very important by the referees.

The Hot Papers are articles that the Editors have chosen on the basis of the referee reports to be of particular importance for an intensely studied area of research.

Check out these journals:

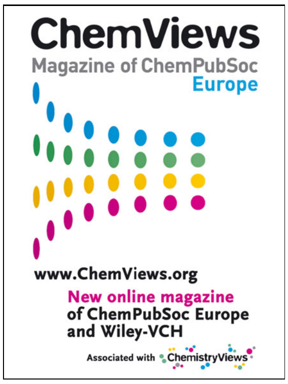


www.chemasianj.org



www.chemcatchem.org

www.chempluschem.org



www.chemviews.org

© 2013 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim