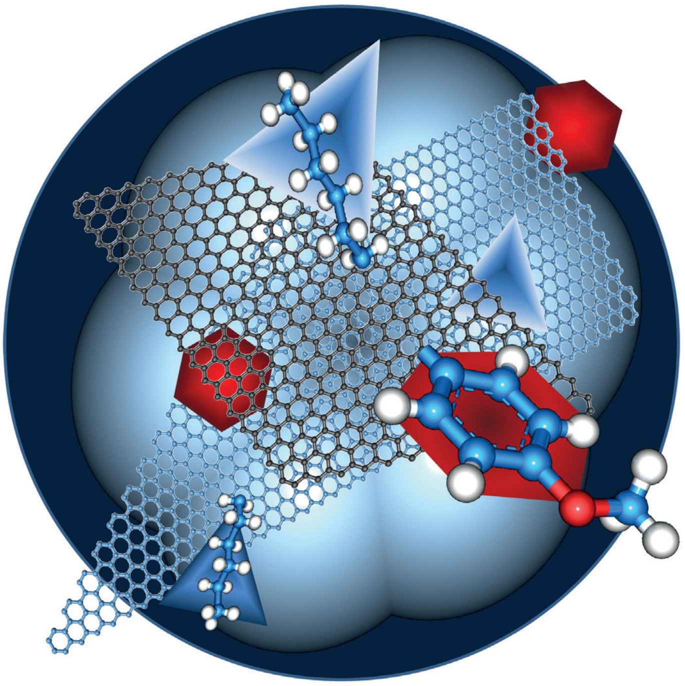
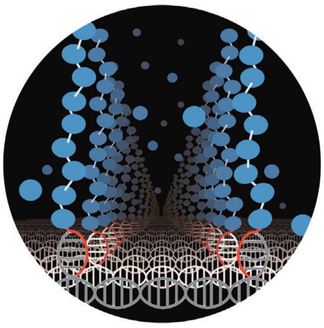
Understanding the chemistry …

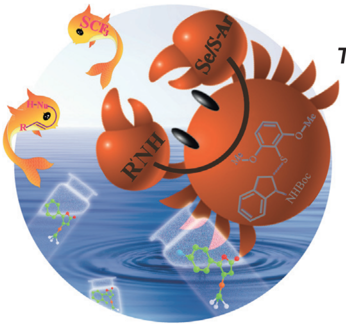


… of graphene will play an important role in the design of complex graphene architectures. In their Communication on page 5861 ff., A. Hirsch and co-workers describe the functionalization of individual graphene sheets deposited on surfaces and bulk functionalization in dispersion. This approach, based on the interplay between functionalization and retrofunctionalization, allows double- and single-sided bisfunctionalization of individual layers.



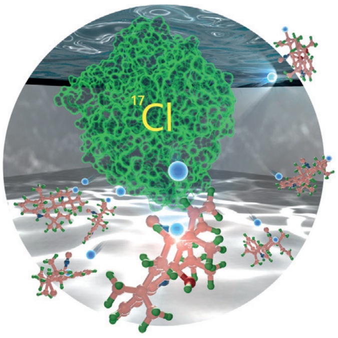
DNA Nanotechnology

Surface-initiated polymerization reactions on DNA origami that enable the precise design of nanopatterned polymers are described by T. Weil, Y. Wu, and co-workers in their Communication on page 5692 ff.



Trifluoromethylthiolation

A bifunctional chiral sulfide catalyst and a shelf-stable electrophilic SCF_3 reagent are used for the enantioselective trifluoromethylthiolating lactonization that is reported by X. Zhao et al. in their Communication on page 5846 ff.



Halogenases

In their Communication on page 5780 ff., X. Liu et al. present a novel halogenase capable of selectively chlorinating seven structurally distinct ambiguine, fischerindole, and hapalindole alkaloids by late-stage C–H functionalization.

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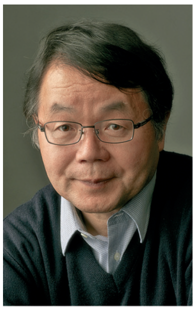
Service

Author Profile

"The principal aspect of my personality is I am always optimistic.
My favorite painter is Alfred Sisley …"
This and more about Norihiro Tokitoh can be found on page 5634.

News



H. Hosono

S. Murai

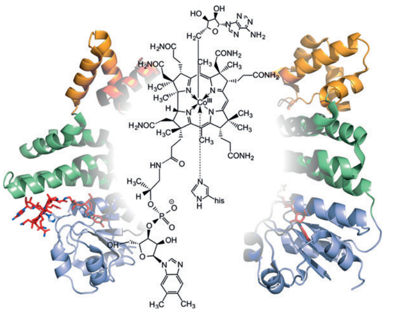
S. Maeda

Highlights

Photoswitching

K. Gruber,* B. Kräutler* ____ **5638 – 5640**

Coenzyme B_{12} Repurposed for Photoregulation of Gene Expression



Old cofactor, new tricks: In enzymes, coenzyme B_{12} has a well-known function as a radical initiator through homolysis of the Co–C bond. It has recently been shown that nature has repurposed this cofactor as a photosensitive switch for the regulation of bacterial carotenoid biosynthesis. Co–C bond breakage is again the key event in this process, triggering huge conformational changes in the B_{12}-binding protein.

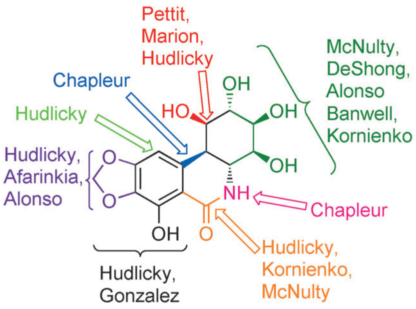
Reviews

Natural Products

M. Ghavre, J. Froese, M. Pour, T. Hudlicky* ____ **5642 – 5691**

Synthesis of Amaryllidaceae Constituents and Unnatural Derivatives

The extracts of plants of the Amaryllidaceae family contain a class of isocarbostyril natural products that are well known to have potent anti-cancer activity (see for example, (+)-pancratistatin). Recent total syntheses of these natural products and their derivatives are summarized. The structure–activity relationships are also discussed and guidelines for the future modifications are formulated.



Structural modifications in the pharmacophore of (+)-pancratistatin

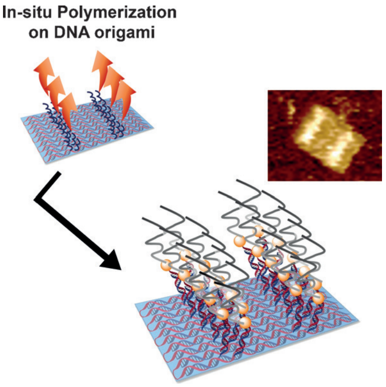
Communications

DNA Nanotechnology

Y. Tokura, Y. Jiang, A. Welle, M. H. Stenzel, K. M. Krzemien, J. Michaelis, R. Berger, C. Barner-Kowollik, Y. Wu,* T. Weil* ____ **5692 – 5697**

Bottom-Up Fabrication of Nanopatterned Polymers on DNA Origami by In Situ Atom-Transfer Radical Polymerization

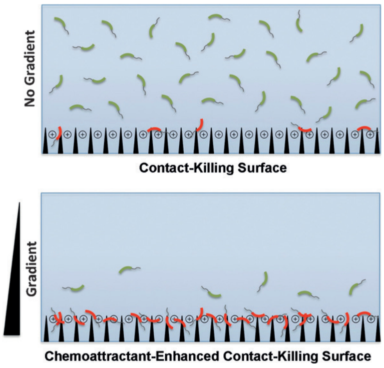
Surface-initiated polymerization reactions on DNA origami enable the precise design of nanopatterned polymers. Characterization by atomic force microscopy, gel electrophoresis, and time-of-flight secondary-ion mass spectrometry showed that this approach can be used to fabricate polymers of different patterns and lengths on the nanoscale.



Frontispiece

For the USA and Canada:
ANGEWANDTE CHEMIE International Edition (ISSN 1433-7851) is published weekly by Wiley-VCH, PO Box 101161, 69451 Weinheim, Germany. US mailing agent: SPP, PO Box 437, Emigsville, PA 17318. Periodicals postage paid at Emigsville, PA. US POSTMASTER: send address changes to *Angewandte Chemie*, John Wiley & Sons Inc., C/O The Sheridan Press, PO Box 465, Hanover, PA 17331. Annual subscription price for institutions: US$ 16.862/14.051 (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.

Like a moth to a flame: The activity of an antimicrobial surface coated with a biocidal agent that can kill microbes upon contact (contact-killing surface) can be enhanced substantially by using a chemoattractant (CA) concentration gradient to attract bacteria. This concept is demonstrated using two non-biocidal CAs (aspartate, glucose) to attract common foodborne bacteria to a silane-coated surface. Live bacteria = green; dead bacteria = red.



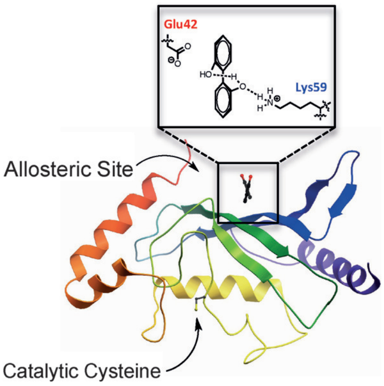
Antimicrobial Surfaces

R. Jain, N. G. Faith, A. Milkowski,
K. Nelson, D. Busche, D. M. Lynn,
C. J. Czuprynski,
N. L. Abbott* ———— **5698 – 5702**

Using Chemoattractants to Lure Bacteria to Contact-Killing Surfaces

---

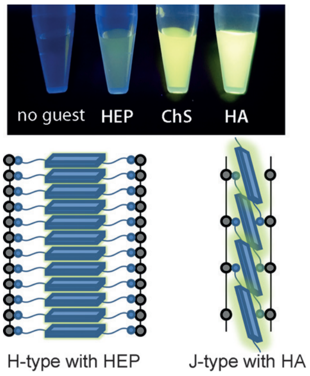
From a distance: Allosteric regulation of enzyme activity is an attractive avenue in chemical biology, but is often difficult to achieve. Two small-molecule inhibitors of the SUMO E2 enzyme Ubc9 were discovered through an X-ray crystallographic fragment screen to bind to a previously unknown allosteric site distal to the active site. This interaction and its effect on SUMOylation activity are discussed.



Allosteric Inhibitors

W. M. Hewitt, G. T. Lountos,
K. Zlotkowski, S. D. Dahlhauser,
L. B. Saunders, D. Needle, J. E. Tropea,
C. Zhan, G. Wei, B. Ma, R. Nussinov,
D. S. Waugh,
J. S. Schneekloth, Jr.* ———— **5703 – 5707**

Insights Into the Allosteric Inhibition of the SUMO E2 Enzyme Ubc9



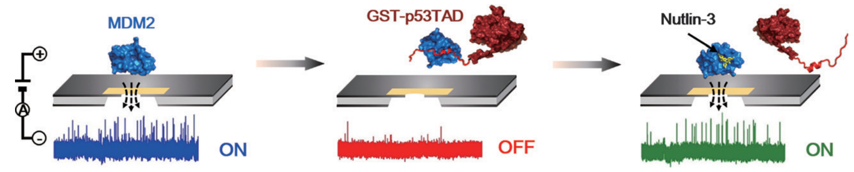
An unexpectedly selective fluorescent (FL) chemosensor for hyaluronic acid (HA) was developed, where structural information on the target critically directs the mode of chemosensor self-assembly leading to the characteristic FL response (see picture). This system is potentially applicable to the clinical diagnosis of functional disorders such as cancer-related diseases involving the overexpression of HA.

Fluorescent Probes

T. Noguchi,* B. Roy, D. Yoshihara,
J. Sakamoto, T. Yamamoto,
S. Shinkai* ———— **5708 – 5712**

Emergent Molecular Recognition through Self-Assembly: Unexpected Selectivity for Hyaluronic Acid among Glycosaminoglycans

---



Sieving for protein interactions: The protein–protein interaction between MDM2 and the p53 transcriptional activation domain (GST-p53TAD), and its inhibition by Nutlin-3, could be detected using a low-noise solid-state nanopore. This nanopore system could aid high-throughput screening for other protein–protein interaction inhibitors.

Protein–Protein Interactions

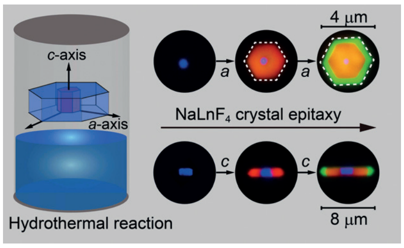
D.-K. Kwak, H. Chae, M.-K. Lee, J.-H. Ha,
G. Goyal, M. J. Kim, K.-B. Kim,*
S.-W. Chi* ———— **5713 – 5717**

Probing the Small-Molecule Inhibition of an Anticancer Therapeutic Protein-Protein Interaction Using a Solid-State Nanopore

Multicolor Microcrystals

Y. Zhang, L. Huang,* X. Liu* **5718 – 5722**

Unraveling Epitaxial Habits in the $NaLnF_4$ System for Color Multiplexing at the Single-Particle Level

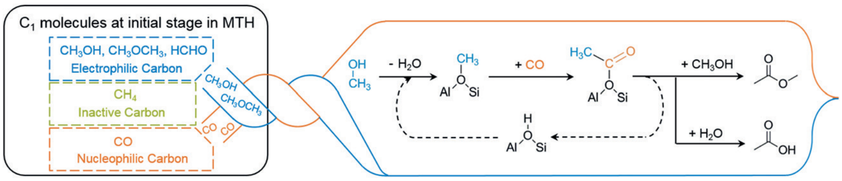


Pimp my particles: Fine control of crystal epitaxial growth was achieved with a $NaLnF_4$ system by using a modified hydrothermal method. On the basis of kinetic and thermodynamic investigations, it is shown that by precisely controlling shell thickness and growth orientation it is possible to grow microparticles with multicolor emitting capabilities at the single-particle level.

Catalytic Mechanisms

Y. Liu, S. Müller, D. Berger, J. Jelic, K. Reuter, M. Tonigold, M. Sanchez-Sanchez,* J. A. Lercher* **5723 – 5726**

Formation Mechanism of the First Carbon–Carbon Bond and the First Olefin in the Methanol Conversion into Hydrocarbons



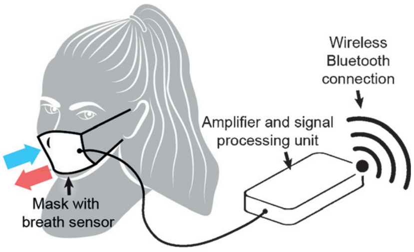
Who's first? Combining kinetics, spectroscopy, and DFT calculations shows the first carbon–carbon bond in the methanol-to-hydrocarbons reaction is formed through the carbonylation of methanol or dimethyl ether, generating acetic acid and methyl acetate. Olefins arise as secondary products from these acetyl species.

Sensor Technology

F. Güder, A. Ainla, J. Redston, B. Mosadegh, A. Glavan, T. J. Martin, G. M. Whitesides* **5727 – 5732**

Paper-Based Electrical Respiration Sensor

Internet-enabled paper-based sensor: A simple paper-based sensor relying on changes in the humidity caused by breathing was fabricated (see picture). The electrical conductivity of the cellulose adsorbent varied as it was loaded with water from humid exhaled air.

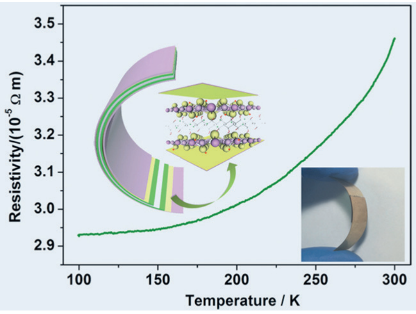


Electrical Conductors

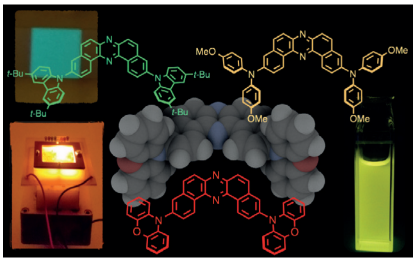
X. Hu, W. Shao, X. D. Hang, X. D. Zhang,* W. G. Zhu, Y. Xie* **5733 – 5738**

Superior Electrical Conductivity in Hydrogenated Layered Ternary Chalcogenide Nanosheets for Flexible All-Solid-State Supercapacitors

Metallic nanosheets: The conductivity of the layered ternary chalcogenide Cu_2WS_4 is switched from semiconducting to metallic by hydrogen incorporation, accompanied by a strong increase in conductivity. The metallic hydrogenated-Cu_2WS_4 nanosheets were applied as electrode material in an all-solid-state flexible supercapacitor.

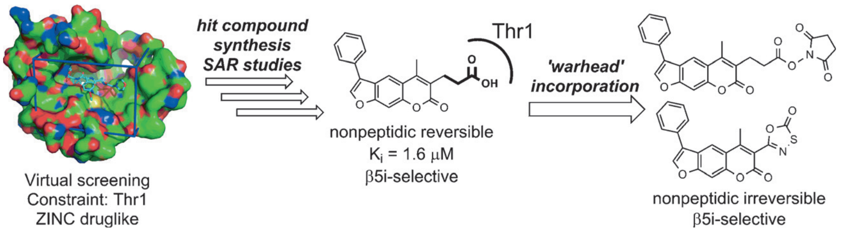


Organic Electronics



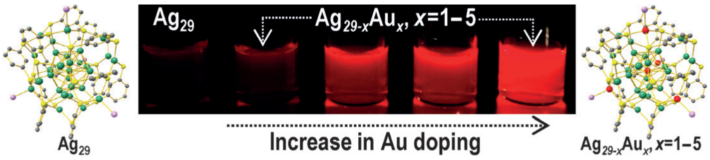
Photophysics: A series of U-shaped donor–acceptor–donor emissive compounds based on the electron-accepting unit dibenzo[*a,j*]phenazine has been developed. Static and dynamic photophysical investigations of these compounds revealed their detailed thermally activated delayed fluorescence properties. The external quantum efficiency of the organic light-emitting diodes fabricated with the new materials reached values up to 16%.

Inhibitors



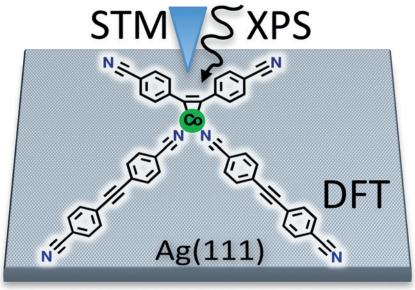
Small and mighty: Nonpeptidic reversible inhibitors that selectively block the chymotrypsin-like (β5i) subunit of the human immunoproteasome were discovered, and derivatives that act irreversibly through covalent inhibition were designed. These small-molecule inhibitors display high subunit selectivity and no cytotoxicity, and they discriminate between the immunoproteasome and the constitutive proteasome in cell-based assays.

Metal Nanoclusters



The photoluminescence quantum yield (QY) of a weakly luminescent Ag_{29} nanocluster was 26-fold enhanced by doping the nanocluster with a distinct number of gold atoms, while the original Ag_{29} framework was kept intact. A detailed characterization showed the presence of Au heteroatoms replacing the silver atom at the center of the Ag_{29} nanocluster and the atoms at the four phosphine binding sites of Ag_{29}, which play a pivotal role in the QY enhancement mechanism.

Surface Chemistry

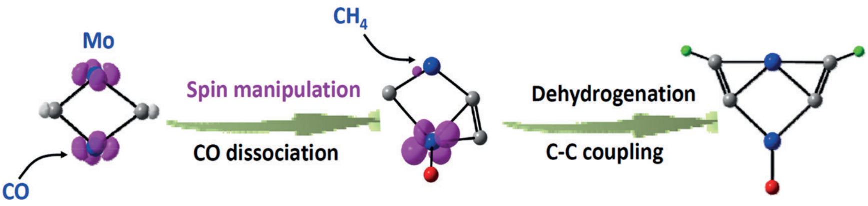


Organocobalt complexation at the single-molecule level: Scanning tunneling microscopy (STM) and X-ray photoelectron spectroscopy (XPS) supported by density functional theory (DFT) calculations were used to obtain atomistic insight into the formation and nature of an unprecedented organocobalt complex at a solid–vacuum interface, specifically on the Ag(111) surface.

Methane Activation

Q.-Y. Liu, J.-B. Ma,* Z.-Y. Li, C. Zhao, C.-G. Ning, H. Chen,* S.-G. He* ________ 5760 – 5764

Activation of Methane Promoted by Adsorption of CO on $Mo_2C_2^-$ Cluster Anions

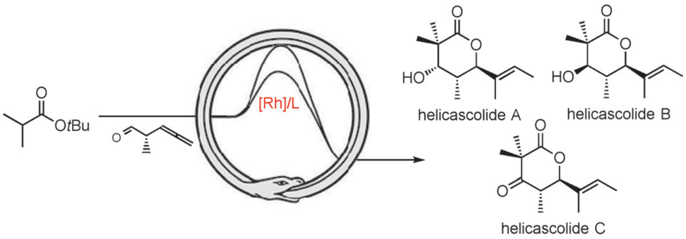


Dissociative adsorption of CO onto the $Mo_2C_2^-$ cluster anion tunes down the spin density distribution on one Mo atom that is then able to activate methane under thermal collision conditions through oxidative addition. Dehydrogenation product has been observed and C–C coupling is predicted.

Natural Products

A. M. Haydl, D. Berthold, P. A. Spreider, B. Breit* ________ 5765 – 5769

Stereodivergent and Protecting-Group-Free Synthesis of the Helicascolide Family: A Rhodium-Catalyzed Atom-Economical Lactonization Strategy

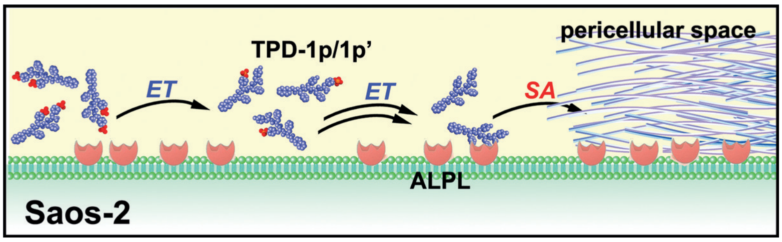


All in the family: The natural product family of the helicascolides A–C are one of countless groups of natural products containing six-membered lactones in their core structure. The rhodium-catalyzed regio- and diastereoselective addition of carboxylic acids with allenes permits the atom-economic and highly diastereoselective synthesis of the lactone core and allows for rapid access to this product family.

Anticancer Therapeutics

J. Zhou, X. W. Du, B. Xu* ________ 5770 – 5775

Regulating the Rate of Molecular Self-Assembly for Targeting Cancer Cells

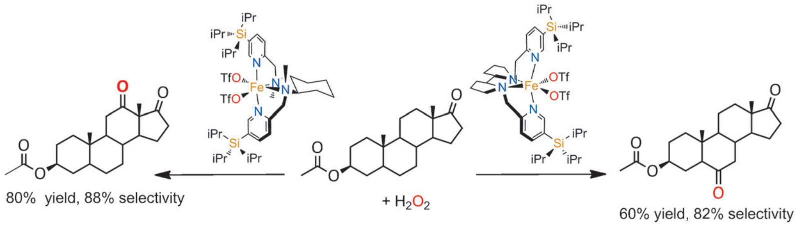


Tailoring the number of phosphates on a peptidic substrate enables regulation of the rate of self-assembly of the enzyme reaction product. Such a rate regulation allows selective inhibition of osteosarcoma cells over hepatocytes, which constitutes a promising approach to target cancer cells in a specific organ.

Bioinspired Catalysis

D. Font, M. Canta, M. Milan, O. Cussó, X. Ribas, R. J. M. Klein Gebbink,* M. Costas* ________ 5776 – 5779

Readily Accessible Bulky Iron Catalysts exhibiting Site Selectivity in the Oxidation of Steroidal Substrates



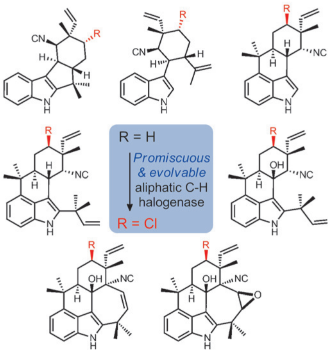
Iron oxidizes: Iron complexes with bulky silyl substituents catalyze the site-selective oxidation of alkyl C–H bonds with H_2O_2 under mild conditions. For example, unprecedented site-selective oxidation at C6 and C12 methylenic sites in steroidal substrates is shown to be governed by the chirality of the catalysts.

Biosynthesis and Biocatalysis

M. L. Hillwig, Q. Zhu, K. Ittiamornkul, X. Liu* ———— 5780 – 5784

Discovery of a Promiscuous Non-Heme Iron Halogenase in Ambiguine Alkaloid Biogenesis: Implication for an Evolvable Enzyme Family for Late-Stage Halogenation of Aliphatic Carbons in Small Molecules

Back Cover

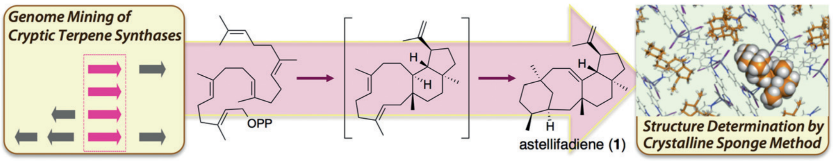


The AmbO5 halogenase is found to selectively chlorinate seven structurally distinct ambiguine, fischerindole, and hapalindole alkaloids by late-stage aliphatic C—H group functionalization. The characterization of a C-terminal sequence motif in AmbO5 important for substrate tolerance and specificity provides evidence on the evolvable nature of this newly discovered halogenase family towards small molecules.

Natural Products

Y. Matsuda, T. Mitsuhashi, S. Lee, M. Hoshino, T. Mori, M. Okada, H. Zhang, F. Hayashi, M. Fujita,* I. Abe* ———— 5785 – 5788

Astellifadiene: Structure Determination by NMR Spectroscopy and Crystalline Sponge Method, and Elucidation of its Biosynthesis

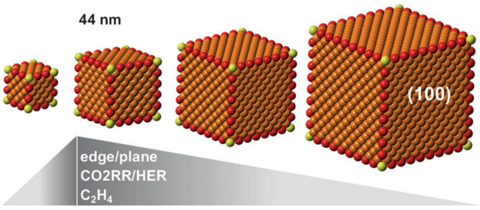


A unique tetracyclic fungal sesterterpene: Genome mining and heterologous expression of a cryptic fungal terpene synthase provided astellifadiene (**1**) with an unprecedented 6-8-6-5-fused ring system. The structure of **1** was unambiguously determined by the crystalline sponge method coupled with NMR analyses. Further, the biosynthesis of **1** was proposed on the basis of the isotope-incorporation experiments performed both in vivo and in vitro.

CO_2 Reduction

A. Loiudice, P. Lobaccaro, E. A. Kamali, T. Thao, B. H. Huang, J. W. Ager, R. Buonsanti* ———— 5789 – 5792

Tailoring Copper Nanocrystals towards C_2 Products in Electrochemical CO_2 Reduction

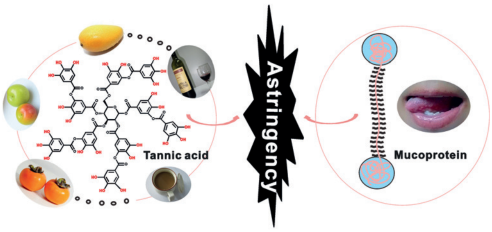


On the edge: Cu nanocrystal cubes and spheres with different sizes were synthesized by means of colloidal chemistry. The highest selectivity towards the CO_2 reduction reaction (CO2RR) and ethylene was found in Cu cubes with 44 nm edge length. The size-dependent trend of the catalytic activity suggests the key role played by edge sites in CO2RR.

Surface Chemistry

S. H. Ma, H. Lee, Y. M. Liang, F. Zhou* ———— 5793 – 5797

Astringent Mouthfeel as a Consequence of Lubrication Failure

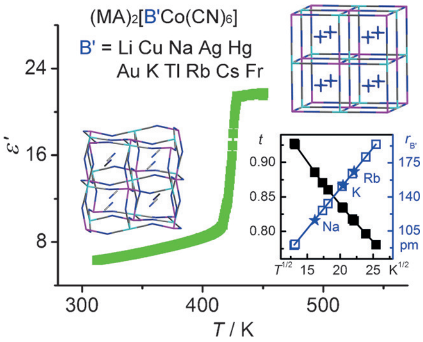


Astringent mouthfeel sensation on the tongue was experimentally demonstrated to originate from the lubrication failure because of the weak interaction between polyphenolic molecules and lubricious protein. This observation resulted in the development of tongue-simulating hydrogels and tannic-acid-releasing gloves.

Dielectric Transitions

C. Shi, C.-H. Yu, W. Zhang* **5798 – 5802**

Predicting and Screening Dielectric Transitions in a Series of Hybrid Organic–Inorganic Double Perovskites via an Extended Tolerance Factor Approach

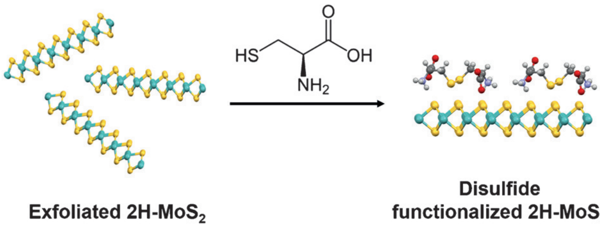


Goldschmidt tolerance factor *t* is extended to the hybrid double perovskites $(MA)_2$-$[B'B''(CN)_6]$ (MA = methylammonium cation) to predict and screen dielectric transitions in 121 compounds through the correlations among *t*, the radius of the B component and the transition temperature.

Surface Functionalization

X. Chen, N. C. Berner, C. Backes, G. S. Duesberg, A. R. McDonald* **5803 – 5808**

Functionalization of Two-Dimensional MoS_2: On the Reaction Between MoS_2 and Organic Thiols

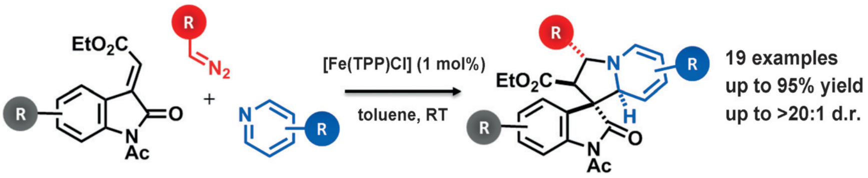


An unexpected appendage: In the functionalization of 2D MoS_2 with organic thiols, thiols were oxidized to disulfides, rather than coordinating at S-vacancies on the MoS_2 surface, as originally conceived. The oxidation was facilitated by MoS_2, resulting in a high density of organic disulfides docked on the MoS_2 surface.

Multicomponent Reactions

J. Day, B. McKeever-Abbas, J. Dowden* **5809 – 5813**

Stereoselective Synthesis of Tetrahydroindolizines through the Catalytic Formation of Pyridinium Ylides from Diazo Compounds

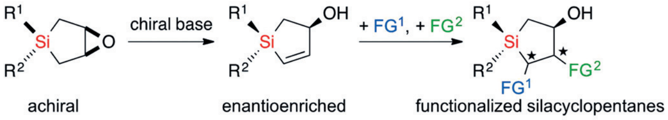


Lost and found: Commercially available Fe^{III} and Cu^{I} complexes catalyzed the efficient multicomponent cycloaddition of diazo compounds, pyridines, and electrophilic alkenes to give alkaloid-inspired tetrahydroindolizidines with high diastereoselectivity (see scheme). The catalytic formation of versatile pyridinium ylides from metal carbenes, until now poorly developed, sets the stage for the invention of further multicomponent reactions in future.

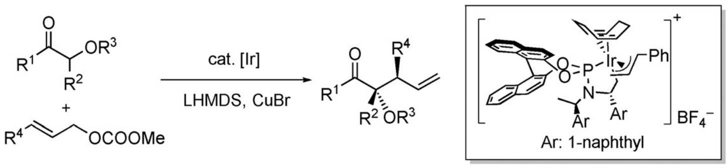
VIP Asymmetric Synthesis

K. Igawa,* D. Yoshihiro, Y. Abe, K. Tomooka* **5814 – 5818**

Enantioselective Synthesis of Silacyclopentanes



Silacyclopentene oxides were converted into functionalized silacyclopentanes by highly enantioselective β-elimination followed by various stereospecific transformations. The reaction mechanism of the β-elimination was analyzed by DFT calculations. A hydroxy-substituted silacyclopentane showed substantial binding to a serotonin receptor protein in an in vitro assay.



Side by side: The title reaction is catalyzed by a metallacyclic iridium complex to form products containing two contiguous stereogenic centers, one derived from the nucleophile and one from the electrophile. These reactions occur between allyl methyl carbonates and unstabilized copper(I) enolates generated in situ from acyclic α-alkoxy ketones. The resulting products can be readily converted into enantioenriched tertiary alcohols and tetrahydrofuran derivatives.

Asymmetric Catalysis

X. Jiang, W. Chen,
J. F. Hartwig* ——— **5819–5823**

Iridium-Catalyzed Diastereoselective and Enantioselective Allylic Substitutions with Acyclic α-Alkoxy Ketones

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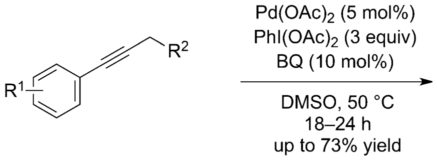

Combating oxygen deficiency: A one-step protocol has been developed for the palladium-catalyzed conversion of simple alkynes into α-acetoxylated enones under oxidative conditions (see scheme; BQ = 1,4-benzoquinone). A wide range of functional groups are tolerated in the reaction. Mechanistic studies with [^{18}O]DMSO revealed that the ketone oxygen atom in the product originates from DMSO.

Synthetic Methods

T. Jiang, X. Quan, C. Zhu, P. G. Andersson,
J.-E. Bäckvall* ——— **5824–5828**

Palladium-Catalyzed Oxidative Synthesis of α-Acetoxylated Enones from Alkynes

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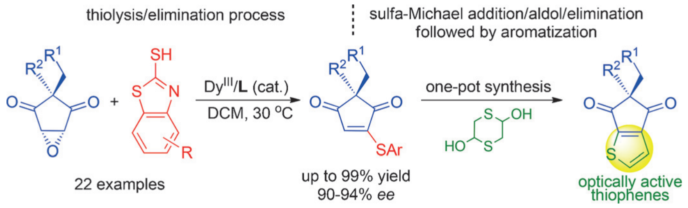

Cap it all: The title reaction of *meso*-diketoepoxides with 2-mercaptobenzothiazoles has been realized. An array of cyclopentene-1,3-diones bearing an all-carbon quaternary stereogenic center were obtained in high yield and excellent enantioselectivity. This methodology paves the way for the construction of optically active thiophenes.

Asymmetric Catalysis

L. Yao, Q. Zhu, L. Wei, Z.-F. Wang,
C.-J. Wang* ——— **5829–5833**

Dysprosium(III)-Catalyzed Ring-Opening of *meso*-Epoxides: Desymmetrization by Remote Stereocontrol in a Thiolysis/ Elimination Sequence

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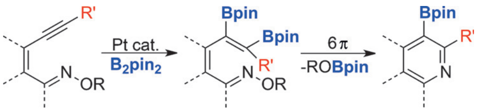


Get in the ring! β-Alkynyl α,β-unsaturated oximes undergo a alkyne diboration/ 6π-electrocyclization sequence to deliver a range of pyridine boronic acid derivatives. The scope of this method to deliver useful heterocyclic products is described.

Synthetic Methods

H. Mora-Radó, L. Bialy, W. Czechtizky,
M. Méndez, J. P. A. Harrity* **5834–5836**

An Alkyne Diboration/ 6π-Electrocyclization Strategy for the Synthesis of Pyridine Boronic Acid Derivatives

Cross-Coupling

Y.-L. Xiao, Q.-Q. Min, C. Xu, R.-W. Wang, X. Zhang* —— 5837 – 5841

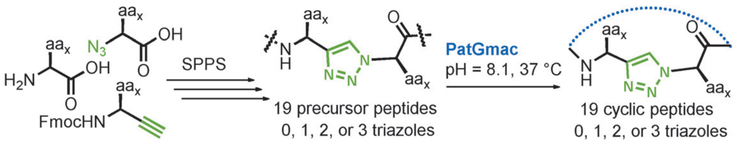
Nickel-Catalyzed Difluoroalkylation of (Hetero)Arylborons with Unactivated 1-Bromo-1,1-difluoroalkanes

Ligand combo: The title reaction requires the use of a combined (2+1) ligand system, that is, a combination of a bi- and monodentate ligand (4,4′-di*t*Bu-bpy + DMAP). This system allows employment of a wide range of unactivated 1-bromo-1,1-difluoroalkanes as coupling partners, thus providing a highly efficient method for applications in drug discovery and development. bpy = bipyridine, DMAP = 4-(*N*,*N*-dimethylamino)pyridine.

Cyclic Peptides

E. Oueis, M. Jaspars, N. J. Westwood, J. H. Naismith* —— 5842 – 5845

Enzymatic Macrocyclization of 1,2,3-Triazole Peptide Mimetics



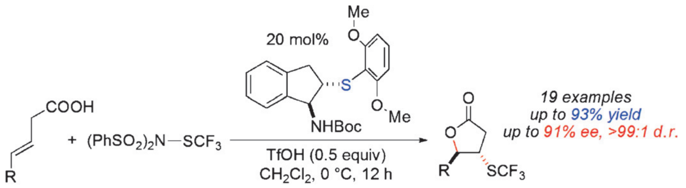
The macrocyclase enzyme PatGmac from the patellamide pathway of the cyanobactin family successfully macrocyclized non-natural peptides where one, two, or three 1,4-substituted 1,2,3-triazole rings were incorporated at different positions of the core peptide. 19 cyclic peptides were macrocyclized by PatGmac, among which 9 were isolated and fully characterized.

Trifluoromethylthiolation

X. Liu, R. An, X. Zhang, J. Luo, X. Zhao* —— 5846 – 5850

Enantioselective Trifluoromethylthiolating Lactonization Catalyzed by an Indane-Based Chiral Sulfide

Inside Back Cover



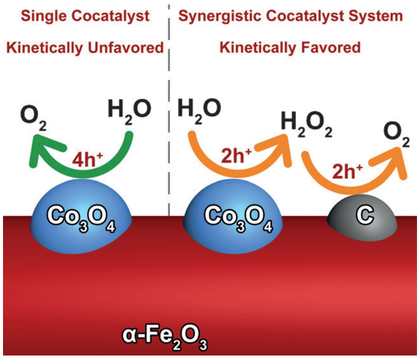
An efficient approach for enantioselective trifluoromethylthiolating lactonization entails the use of an indane-based bifunctional chiral sulfide catalyst and a new shelf-stable electrophilic SCF_3 reagent. This transformation represents the first enantioselective trifluoromethylthiolation that is enabled by a catalyst with a Lewis basic sulfur center.

Water Splitting

P. Zhang, T. Wang, X. Chang, L. Zhang, J. Gong* —— 5851 – 5855

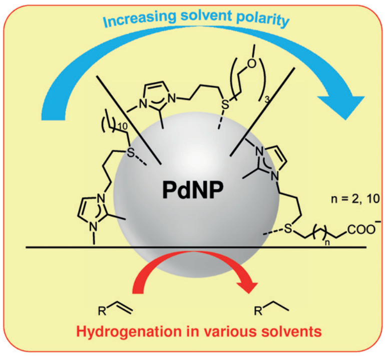
Synergistic Cocatalytic Effect of Carbon Nanodots and Co_3O_4 Nanoclusters for the Photoelectrochemical Water Oxidation on Hematite

Inside Cover



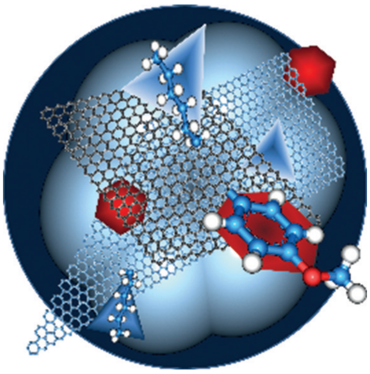
Cat and co: The photocurrent density is enhanced by 78% for the photoelectrochemical water-oxidation on an Fe_2O_3 photoanode when the Fe_2O_3 it is treated with two cocatalysts. The synergistic effect between the carbon nanodot and Co_3O_4 cocatalysts originates from the acceleration of the slow-reaction pathway on Co_3O_4 by a kinetically favored two-step-two-electron water-oxidation mechanism.

Have it your way! A bidentate hybrid NHC-thioether ligand for stabilizing palladium nanoparticles is presented. The modular approach allows the rapid and easy synthesis of various ligands, depending on the solvent of choice. XPS was used as an elegant tool for determining the binding mode of the NHC on the nanoparticles and the catalytic activity of the nanoparticles for chemoselective hydrogenation was investigated.



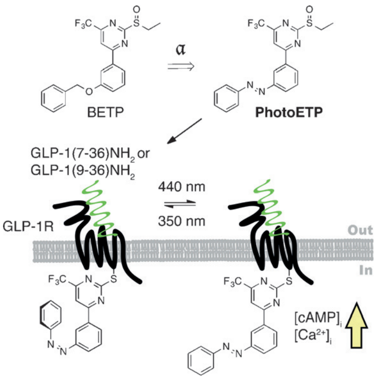
Modified Nanoparticles

Two sides to the story: The use of two consecutive reduction and covalent addition steps leads to the monotopic and ditopic functionalization of individual graphene layers on substrates (one side blocked) as well as graphene in dispersion (both sides accessible).



Graphene Functionalization

Blues and twos: An “azologue” of BETP, a ligand-dependent allosteric activator of the glucagon-like peptide-1 receptor, acts as a synthetic photoswitch. This allows the levels of cAMP, Ca^{2+}, and insulin to be optically controlled in living cells by using blue light.



Photopharmacology

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