VIP *The following Communications have been judged by at least two referees to be "very important papers" and will be published online at www.angewandte.org soon:*

Editorial

Author Profile

News

J. K. Barton

P. J. Stang

D. Lentz

R. Dorta

Books

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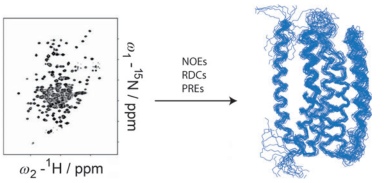
Highlights

Solution NMR Spectroscopy

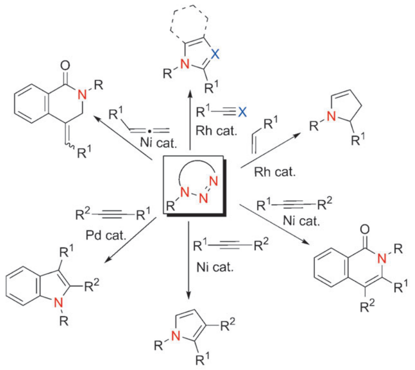
A mastered challenge: The recent solution structures of seven-transmembrane proteins, in particular of proteorhodopsin, have been reported. The structures are a major advance in structural biology and were determined based on experimental restrains derived from nuclear Overhauser effects (NOEs), paramagnetic relaxation enhancements (PREs), and residual dipolar couplings (RDCs, see picture).



Minireviews

Nitrogen Heterocycles

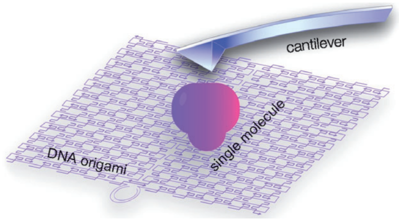
One two three: Transition-metal catalyzed denitrogenative transannulation of 1,2,3-triazole rings has recently received increasing attention as a new concept for the construction of diverse nitrogen-containing heterocyclic cores in a single step (see scheme).



Reviews

Single-Molecule Analysis

Origami for singles: Concurrent to the development of single-molecule analytical techniques has been rapid progress in nanobiotechnology and efforts at building lab-on-a-chip systems for high-throughput analytical biochemistry. The scaffolded DNA origami method is suitable for the construction of defined larger assemblies that can act as a platform for the positioning of various functionalities and their single-molecule analysis (see picture).



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Communications

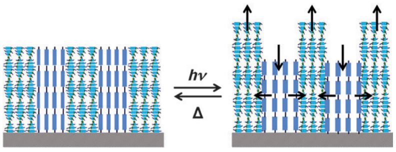
Liquid Crystals

D. Liu,* C. W. M. Bastiaansen,
J. M. J. den Toonder,
D. J. Broer* ________ 892 – 896

Photo-Switchable Surface Topologies in Chiral Nematic Coatings

Frontispiece

An enlightening answer: Dynamic surface photo-responsive topologies of a polymer coating were realized by introducing azobenzene crosslinkers into liquid-crystal polymer networks (see picture). The principle of these coatings is based on breaking the molecular order in the liquid-crystal polymer networks. Under irradiation of UV light the azobenzene compound isomerizes from the *trans* to the *cis* conformation.

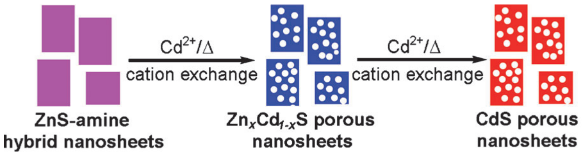


Mesoporous Materials

Y. Yu, J. Zhang, X. Wu, W. Zhao,
B. Zhang* ________ 897 – 900

Nanoporous Single-Crystal-Like $Cd_xZn_{1-x}S$ Nanosheets Fabricated by the Cation-Exchange Reaction of Inorganic–Organic Hybrid ZnS–Amine with Cadmium Ions

Front Cover



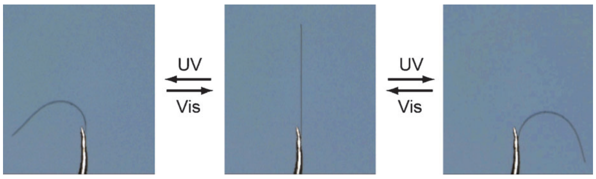
Swapping ions: Nanoporous $Cd_xZn_{1-x}S$ nanosheets with single-crystal-like structure, good structural stability, and tunable pore size and composition have been successfully fabricated by the cation-exchange reaction of prepared ZnS–amine hybrid nanosheets with Cd^{2+} cations (see picture). The porous $Cd_xZn_{1-x}S$ nanosheets are highly active for photocatalytic H_2 evolution from water splitting.

Photochromic Actuators

F. Terao, M. Morimoto,
M. Irie* ________ 901 – 904

Light-Driven Molecular-Crystal Actuators: Rapid and Reversible Bending of Rodlike Mixed Crystals of Diarylethene Derivatives

Inside Cover



Limber but strong: Two-component mixed crystals of diarylethene derivatives exhibit reversible, rapid, and fatigue-resistant bending upon alternate irradiation with UV and visible light (see picture). The crystals showed reversible curling into a hairpin shape while remaining crystalline.

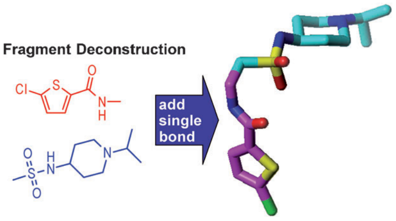
Drug Discovery

M. Nazaré,* H. Matter,* D. W. Will,
M. Wagner, M. Urmann, J. Czech,
H. Schreuder, A. Bauer, K. Ritter,
V. Wehner ________ 905 – 911

Fragment Deconstruction of Small, Potent Factor Xa Inhibitors: Exploring the Superadditivity Energetics of Fragment Linking in Protein–Ligand Complexes

Inside Back Cover

More than just the sum of its parts: The superadditivity effect of fragment linking on ΔG was quantified by deconstructing two fXa inhibitors with congeneric fragments, but different linkers. By connecting both fragments with a single bond, a high linker contribution ΔG_{link} of $-14.0\ \text{kJ mol}^{-1}$ results, which corresponds to an improvement in affinity by around 2.5 orders of magnitude relative to the sum of fragment ΔG values (see picture).



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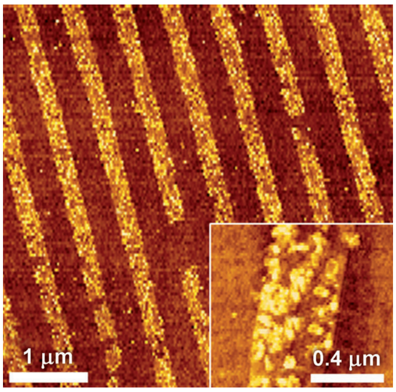


Nanoscale folding of DNA: Taking advantage of facile solution processing, pattern formation under light irradiation, and ready chemical modification of graphene oxide, various patterned films of chemically modified graphene were prepared and employed for spatial patterning of DNA origami structures (see picture). The patterning of DNA origami structures required highly selective adsorption on graphene oxide surfaces.

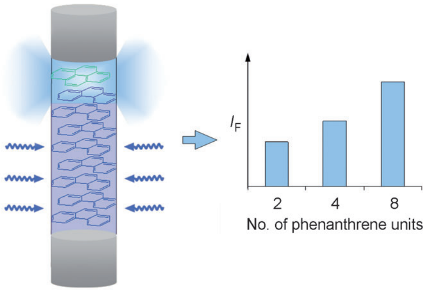
Surface Chemistry

J. M. Yun, K. N. Kim, J. Y. Kim, D. O. Shin, W. J. Lee, S. H. Lee, M. Lieberman,* S. O. Kim* ________ **912–915**

DNA Origami Nanopatterning on Chemically Modified Graphene

Back Cover

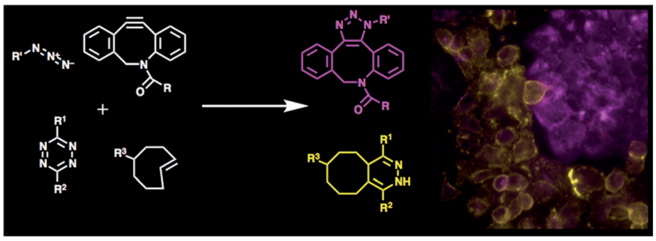
Shedding light on DNA: A DNA-based light-harvesting antenna has been synthesized. Light is absorbed by π-stacked phenanthrene units and efficiently transferred to a phenanthrene–pyrene exciplex. The whole system is structurally organized by a DNA scaffold. Up to eight phenanthrene units are used for light collection and the intensity of the exciplex emission is proportional to the number of light-absorbing chromophores.



Light Harvesting

F. Garo, R. Häner* ________ **916–919**

A DNA-Based Light-Harvesting Antenna



Mutually orthogonal tetrazine–trans-cyclooctene and azide–cyclooctyne cycloaddition reactions were used simultaneously for the bioorthogonal labeling of two different live cell populations in the same culture (see scheme). These small-molecule probes show good chemical reactivity and can be readily incorporated into biological systems.

Double Click Chemistry

M. R. Karver, R. Weissleder, S. A. Hilderbrand* ________ **920–922**

Bioorthogonal Reaction Pairs Enable Simultaneous, Selective, Multi-Target Imaging

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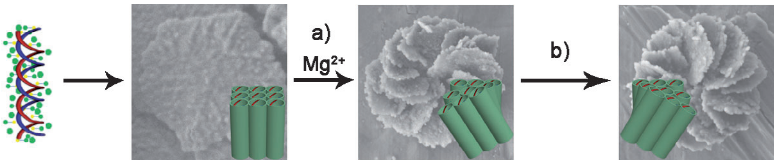


Impeller-like helical DNA–silica complexes (see picture; green: silica) were synthesized in the presence of magnesium ions (a). DNA chiral packing and corresponding macroscopic helical morphologies are tuned by the change of reaction temperature, pH value, and molar ratio (b) of the quaternary ammonium (yellow)/phosphate group.

Asymmetric Biomineralization

B. Liu, L. Han, S. Che* ________ **923–927**

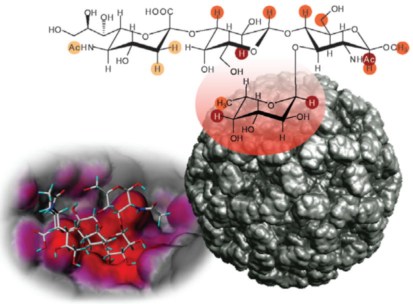
Formation of Enantiomeric Impeller-Like Helical Architectures by DNA Self-Assembly and Silica Mineralization

Virus Host Recognition

B. Fiege, C. Rademacher, J. Cartmell, P. I. Kitov, F. Parra, T. Peters* **928–932**

Molecular Details of the Recognition of Blood Group Antigens by a Human Norovirus as Determined by STD NMR Spectroscopy

Tracing the infection: The binding of human norovirus particles to blood group antigens was investigated using NMR spectroscopy. Binding epitopes were determined at atomic resolution, information on the binding specificity was obtained, and the bioactive conformation of various sugars was revealed. This provides valuable information for the design of entry inhibitors against this important class of human pathogenic viruses.

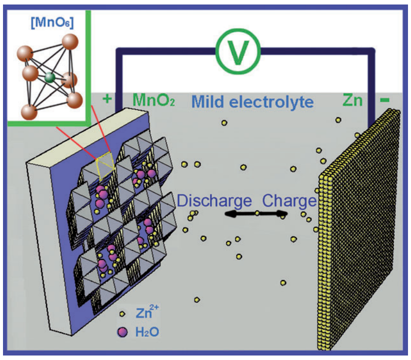


Batteries

C. Xu, B. Li, H. Du, F. Kang* **933–935**

Energetic Zinc Ion Chemistry: The Rechargeable Zinc Ion Battery

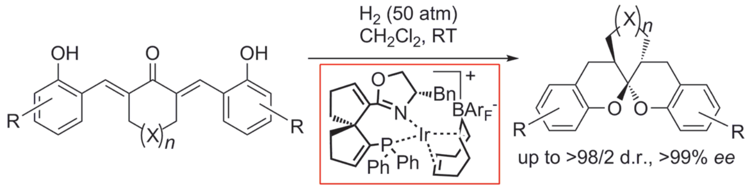
Think zinc: An ideal aqueous energy storage device, referred to as a zinc ion battery, is presented. The device is characterized by high capacity, fast charge/discharge capability, safety, and environmental friendliness. It is composed of an α-MnO_2 cathode, a zinc anode, and a mild $ZnSO_4$ or $Zn(NO_3)_2$ aqueous electrolyte (see scheme). The battery chemistry is based on the migration of Zn^{2+} ions between cathode and anode.



Asymmetric Synthesis

X. M. Wang, Z. B. Han, Z. Wang,* K. Ding* **936–940**

Catalytic Asymmetric Synthesis of Aromatic Spiroketals by SpinPhox/Iridium(I)-Catalyzed Hydrogenation and Spiroketalization of α,α'-Bis(2-hydroxyarylidene) Ketones

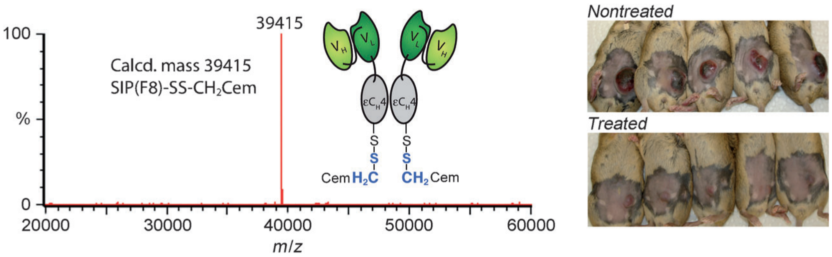


From spiro to spiro: An iridium(I) complex with a spiral P,N ligand (SpinPhox) is highly efficient in the catalytic asymmetric hydrogenation of α,α'-bis(2-hydroxyarylidene) ketones to afford the corresponding aromatic spiroketals in high yields with excellent diastereo- and enantioselectivities (see scheme). The complex plays a dual role in the reaction, acting as catalyst for both the hydrogenation of C=C bonds and the subsequent spiroketalization of bisphenolic ketones.

VIP Cancer Therapy

G. J. L. Bernardes, G. Casi, S. Trüssel, I. Hartmann, K. Schwager, J. Scheuermann, D. Neri* **941–944**

A Traceless Vascular-Targeting Antibody–Drug Conjugate for Cancer Therapy



Right on target: A chemically defined vascular-targeting antibody–drug conjugate (ADC) that offers comprehensive tumor coverage has been developed. When injected intravenously, this ADC potently inhibited tumor growth in a syngeneic immunocompetent model of murine cancer which cannot be cured by conventional cytotoxic agents.

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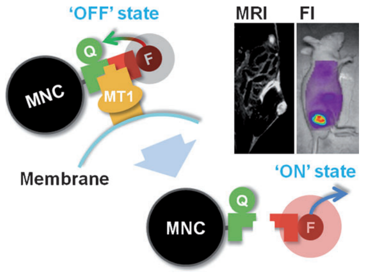
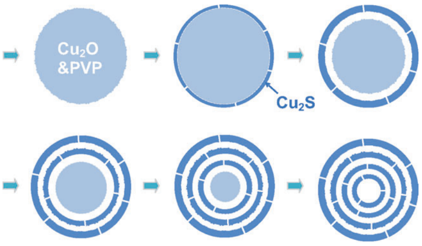


Activatable nanoprobe: A dual-function nanoprobe has been developed that detects membrane type 1-matrix metalloproteinase (MT1-MMP) activity by a dual-signal increase in complementary fluorescence imaging (FI) and magnetic resonance imaging (MRI). MNCs = magnetic nanocrystals, Q = quencher, F = fluorescence dye.

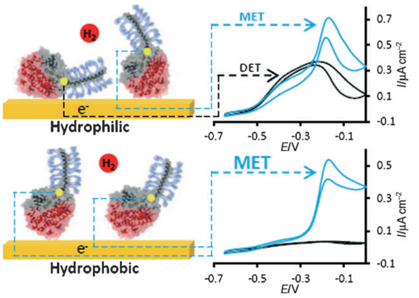
Nanomedicine



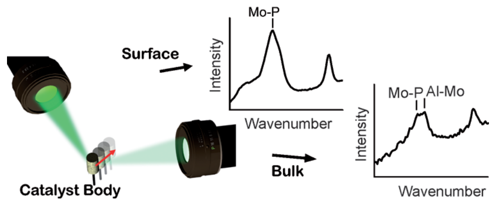
Transformation in a shell: Ion exchange is used for the fabrication of multishelled inorganic hollow materials. The transformation of solid Cu_2O to Cu_2S hollow spheres is investigated as a model reaction (see picture; PVP = poly(vinylpyrrolidone)).

Nanostructured Materials

A transmembrane helix surrounded by detergent molecules close to the surface electron relay is shown, by electrochemical, AFM, and PM-IRRAS studies, to control the orientation of a membrane-bound [NiFe] hydrogenase on electrochemical interfaces. Hence, H_2 oxidation proceeds as a mixture of direct (DET) and mediated electron transfer (MET) on hydrophilic interfaces, but by a MET process on hydrophobic interfaces (see picture).



Enzyme Catalysis



A vibrational fingerprint: A Raman technique has been developed to retrieve spatiotemporal chemical information from millimeter-sized catalyst bodies under preparation. An incipient wetness impregnation of γ-Al_2O_3 catalysts with ammonium heptamolybdate was followed. Diagonal offset Raman spectroscopy was able to distinguish between surface, subsurface, and bulk phase of the catalyst bodies (see picture).

Heterogeneous Catalysis

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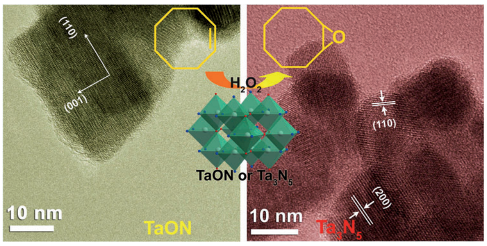
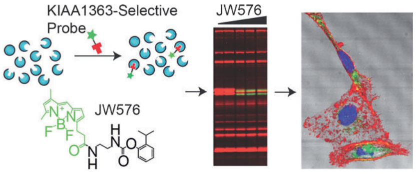
Functional Materials



Touching the surface: Well-defined TaON and Ta_3N_5 nanoparticles were fabricated by a SiO_2-surface-assisted urea method, in which silica catalyzes CN_x formation from urea. Such controlled nitridation endows the nanoparticles with improved activity and tunable selectivity for alkene epoxidation because of the increased electron density around Ta and surface basicity.

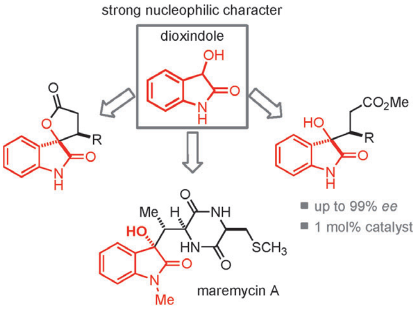
Fluorescent Probes



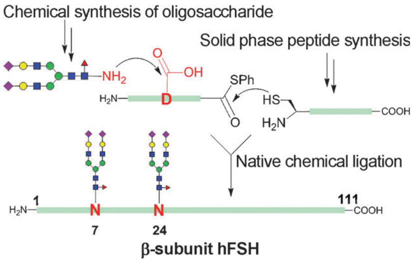
Profiling enzyme activities: A selective, activity-based imaging probe is described for the integral membrane hydrolase KIAA1363 and used to determine the subcellular localization and half-life of this enzyme in human cancer cells (see picture).

Synthetic Methods

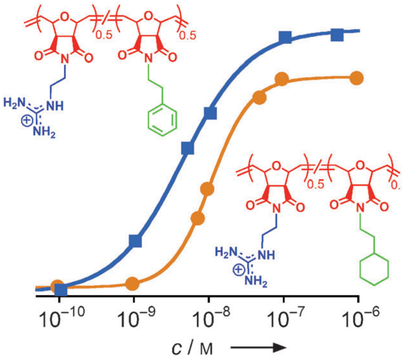
Taming the reactivity: Understanding the nucleophilicity of dioxindole under different reaction conditions is key to a direct and easy access to valuable spiro oxindole γ butyrolactones and 3-substituted 3-hydroxyoxindole derivatives in excellent yields and enantioselectivities (see scheme). The preparation of maremycin A serves as an example for the potential usefulness of this previously unexplored reactivity in natural product synthesis.



Chemical Synthesis of Glycoproteins

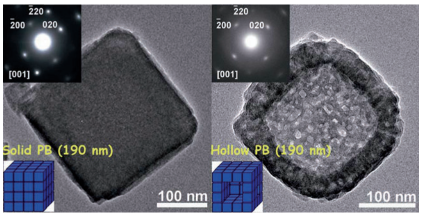


Ambitious undertaking: The β-subunit of the human follicle-stimulating hormone (hFSH) displaying a N-linked consensus sequence oligosaccharide at each of the two wild-type sites was synthesized. The glycoprotein has been designed with acetamidomethyl protected cysteine residues, anticipating folding and association with the α-subunit. This represents the largest realistically glycosylated homogeneous glycoprotein obtained by using strictly chemical methods.



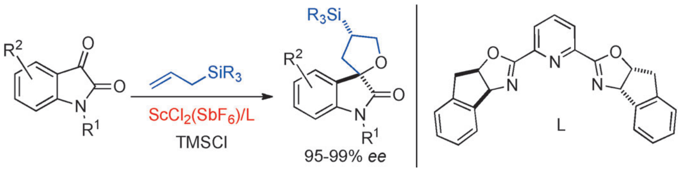
For better or worse: Protein transduction domain mimics built from synthetic polymers demonstrate that aromatic side chains provide better transduction than aliphatic groups at the same relative hydrophobicity. Similarly, a less hydrophobic aromatic side chain is more active than the corresponding aliphatic one containing the same number of carbon atoms (see picture).

Peptidomimetics



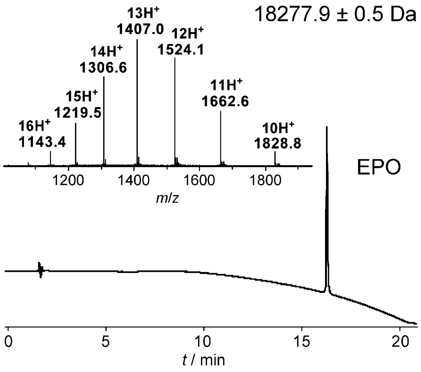
A facile route has been found to prepare Prussian blue (PB) hollow particles with a cubic shape (see picture). With PB mesocrystals used as a starting material, hollow interiors were created through controlled chemical etching in the presence of poly(vinylpyrrolidone). The hollow cavities and particle sizes could be tuned by changing the synthetic conditions, and the original PB crystallinity was preserved even after formation of interior hollows.

Nanoporous Materials



Silyl-inspired spirocycle: The title reaction is the first example of a catalytic asymmetric [3+2] annulation reaction with allylsilanes. The annulation reaction utilizes a chiral $ScCl_2(SbF_6)$/L catalyst and TMSCl as a promoter to afford spirooxindoles in excellent enantioselectivity at room temperature. The Si–C bond can be oxidized to deliver hydroxy-substituted spirooxindoles. TMS = trimethylsilyl.

Synthetic Methods



A new route to EPO: Nonglycosylated human erythropoietin (EPO) was prepared using a convergent chemical ligation synthetic strategy. The synthetic [Lysine^{24,38,83}] EPO analogue, which was purified by HPLC and has the correct molecular weight (see picture), shows well-defined covalent structure, is correctly folded, and is biologically active in a factor-dependent cell line assay.

Chemical Protein Synthesis

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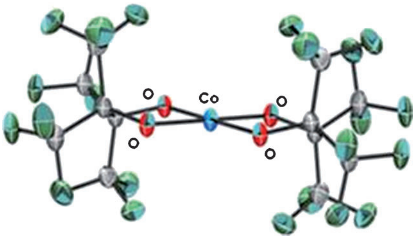
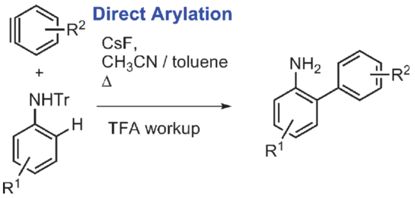
Square-Planar Complexes

It's hip to be square: Two high-spin, square-planar $\{MO_4\}$ complexes are prepared, including the first molecular example with M = Co^{II} (see structure). Structural, spectroscopic, and magnetic susceptibility characterization allows a description of the ligand features required for this highly unusual electronic structure.

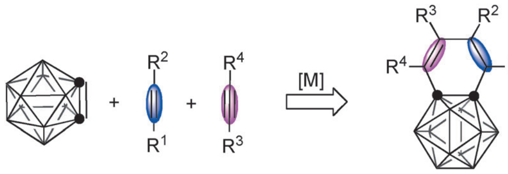


C–H Arylation



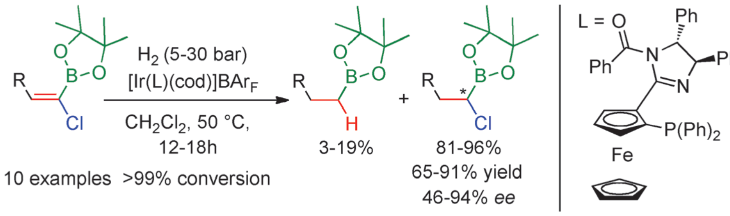
Aryne arylation: A new method of direct arylation is reported for aniline substrates. The reaction uses benzyne to synthesize a variety of aminobiaryls under mild conditions (see scheme), requiring no stoichiometric metalation or transition-metal catalysis. An ene mechanism is implicated, and conveys excellent functional group tolerance relative to metal-mediated processes.

Selective Cycloaddition



Mix three—get one: The complexation of a transition-metal center to an olefin or alkyne can significantly modify its reactivity, which makes the selective coupling of different alkenes or alkynes to carboryne possible. An example of a three-component [2+2+2] cycloaddition reaction of carboryne with unactivated alkene (see scheme, blue) and alkyne (red) mediated by zirconium and nickel complexes is described.

Chemoselective Hydrogenation

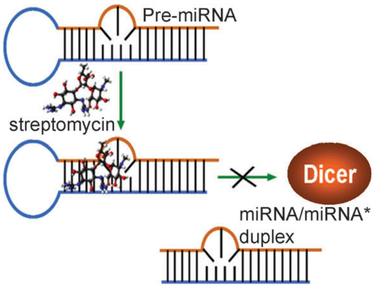


Persistent chlorine: Hydrogenation of borolane-substituted vinylic chlorides catalyzed by Ir–P^N complexes greatly preserved the chlorine substituent on the hydrogenated product, with only 3–19% of dechlorinated byproducts present after hydrogenation. The α-chloro boronic ester products are ideal precursors for proteasome-inhibitor-type anti-cancer drugs, a fact which demonstrates the utility of this hydrogenation method.

Medicinal Chemistry

D. Bose, G. Jayaraj, H. Suryawanshi, P. Agarwala, S. K. Pore, R. Banerjee, S. Maiti* ——— 1019–1023

The Tuberculosis Drug Streptomycin as a Potential Cancer Therapeutic: Inhibition of miR-21 Function by Directly Targeting Its Precursor

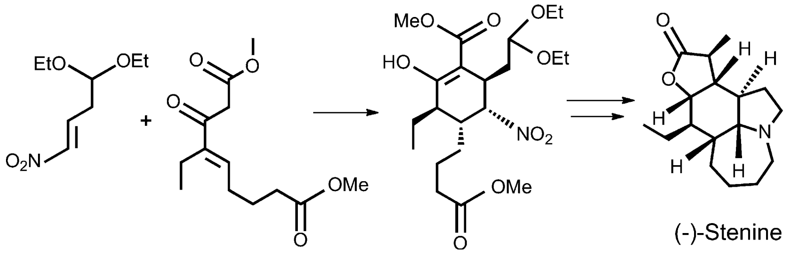


No dice: MicroRNAs (miRNAs) fine-tune gene expression, deregulation of which has been causally associated with a number of debilitating conditions. Streptomycin, a well-known aminoglycoside drug, binds to RNA secondary structures and is shown to inhibit miR-21 function by direct binding to its precursor, thus presumably interfering with the processing by the Dicer enzyme (see scheme).

Total Synthesis

J.-B. Chen, J.-C. Chen, Y. Xie, H.-B. Zhang* ——— 1024–1027

Enantioselective Total Synthesis of (−)-Stenine

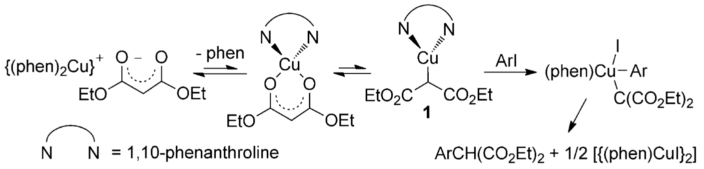


In control: (−)-Stenine has been synthesized in 14 steps from commercially available compounds with an overall yield of 5.9 % by using a method that is based on double Michael addition. In the key step, the stereogenic centers that are required for (−)-stenine are generated in a highly stereocontrolled, asymmetric, one-pot cyclization to give a densely substituted cyclohexane core.

Reaction Mechanisms

Z. Huang, J. F. Hartwig* ——— 1028–1032

Copper(I) Enolate Complexes in α-Arylation Reactions: Synthesis, Reactivity, and Mechanism

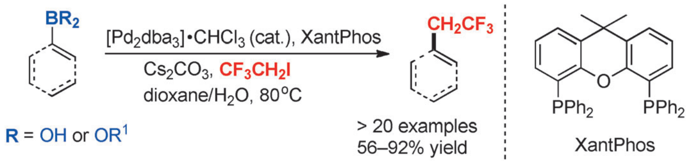


Copper is all bound up: The copper-catalyzed α-arylation of carbonyl compounds occurs through oxidative addition of iodoarenes to the C-bound Cu^{I} enolate species **1** to form an aryl–Cu^{III} intermediate (see scheme). Computational results provide insight into the origins of the relative reactivity of various Cu^{I} enolate complexes in the reactions with iodoarenes.

C–C Coupling

Y. Zhao, J. Hu* ——— 1033–1036

Palladium-Catalyzed 2,2,2-Trifluoroethylation of Organoboronic Acids and Esters



Trifluoroethylation: Aryl boronic acids can be catalytically trifluoroethylated with the readily available reagent CF_3CH_2I (see scheme, dba = dibenzylideneacetone). The reaction tolerates a variety of functional groups and can be extended to the trifluoroethylation of aryl or alkenyl boronic esters. The method is also suitable for the late-stage installation of the CF_3CH_2 group into target molecules.

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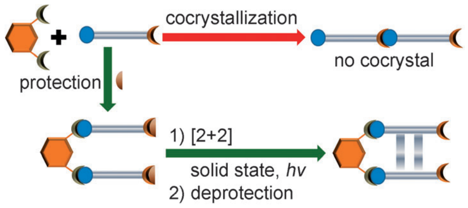
Supramolecular Chemistry

E. Elacqua, P. Kaushik, R. H. Groeneman, J. C. Sumrak, D.-K. Bučar, L. R. MacGillivray* ________ **1037 – 1041**

A Supramolecular Protecting Group Strategy Introduced to the Organic Solid State: Enhanced Reactivity through Molecular Pedal Motion

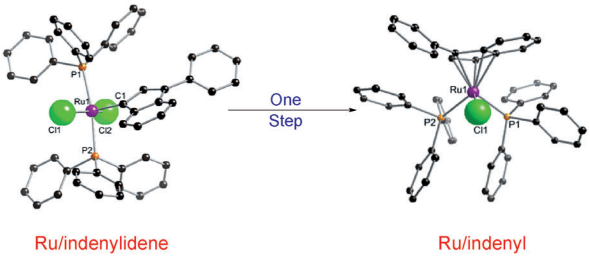


A supramolecular protecting group strategy has been applied to achieve solid-state photodimerizations of olefins lined with a combination of hydrogen-bond-donor and -acceptor groups. Esters were used as protecting groups to generate head-to-head photodimers that were readily converted into diacids. A protected olefin equipped with a stilbene unit exhibits enhanced reactivity that is ascribed to pedal motions in the solid state (orange hexagons: template: blur circles: recognition sites).

Homogeneous Catalysis

S. Manzini, C. A. Urbina-Blanco, A. Poater, A. M. Z. Slawin, L. Cavallo, S. P. Nolan* ____________ **1042 – 1045**

From Olefin Metathesis Catalyst to Alcohol Racemization Catalyst in One Step

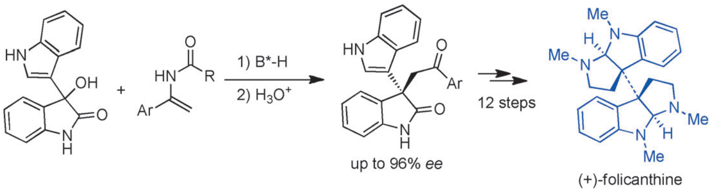


Easy as π: An unusual indenylidene to η^5-indenyl rearrangement of a ruthenium catalyst has been observed. The resulting complex is the formal decomposition product of an olefin metathesis precatalyst that displays exceptional activity in the racemization of chiral alcohols at very low catalyst loadings.

Synthetic Methods

C. Guo, J. Song, J.-Z. Huang, P.-H. Chen, S.-W. Luo, L.-Z. Gong* ______ **1046 – 1050**

Core-Structure-Oriented Asymmetric Organocatalytic Substitution of 3-Hydroxyoxindoles: Application in the Enantioselective Total Synthesis of (+)-Folicanthine

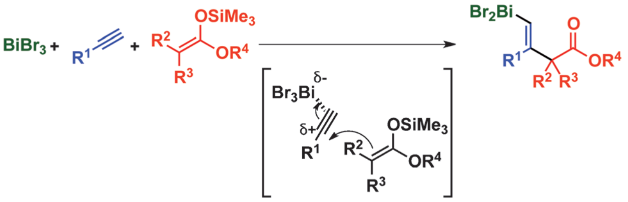


Something constructive: The title reaction involving 3-hydroxyoxindoles gives 3,3′-disubstituted oxindoles with concomitant generation of an all-carbon quaternary stereogenic center in high yield and excellent enantioselectivity. This reaction enabled the enantioselective construction of hexahydropyrroloindole skeletons and the first catalytic enantioselective total synthesis of (+)-folicanthine.

Synthetic Methods

Y. Nishimoto, M. Takeuchi, M. Yasuda, A. Baba* ______________ **1051 – 1054**

Regio- and Stereoselective Carbobismuthination of Alkynes



Three become one: The first carbobismuthination of alkynes has been accomplished by the simple reaction of an alkyne, $BiBr_3$, and a ketene silyl acetal to produce an alkenylbismuth with high stereo- and regioselectivity (see scheme). X-ray crystallographic analysis of the alkenylbismuth product and control experiments using α-bismuthino ester revealed the reaction mechanism.

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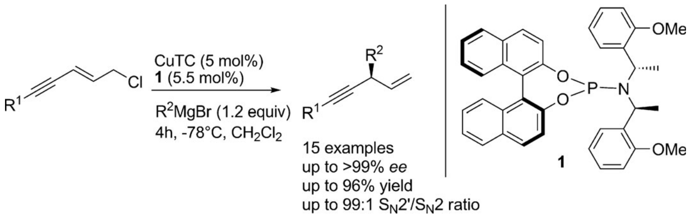
Asymmetric Catalysis

H. Li, A. Alexakis* ________ **1055 – 1058**

Enyne Chlorides: Substrates for Copper-Catalyzed Asymmetric Allylic Alkylation

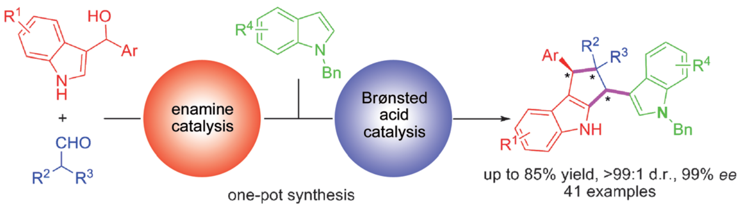


A select few: Several prochiral enyne chlorides were employed as substrates in the title reaction using Grignard reagents as the alkylation reagents (see scheme; CuTC = copper(I) thiophenecarboxylate). Excellent 1,3 substitution regioselectivities and good to excellent enantioselectivities were obtained. The substrate scope is additionally extended to diene chlorides.

One-Pot Syntheses

B. Xu, Z.-L. Guo, W.-Y. Jin, Z.-P. Wang, Y.-G. Peng, Q.-X. Guo* ____ **1059 – 1062**

Multistep One-Pot Synthesis of Enantioenriched Polysubstituted Cyclopenta[*b*]indoles

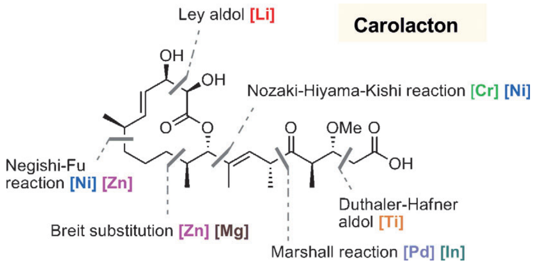


Simple steps, complex result: Consecutive organo-catalyzed reactions of 3-indolylmethanol compounds with aldehydes and N-protected indoles lead to the formation of structurally complex cyclopenta[*b*]indoles (see scheme, Bn = benzyl). These one-pot multistep reactions have a broad substrate scope and give the products in high yields, and with excellent diastereoselectivities and enantioselectivities.

Total Synthesis

T. Schmidt, A. Kirschning* _ **1063 – 1066**

Total Synthesis of Carolacton, a Highly Potent Biofilm Inhibitor



Metals are the key players in the synthesis of caralacton, a strong inhibitor of bacterial biofilms. The total synthesis is based on several metal-mediated key transformations such as the Ley and the Duthaler–Hafner aldol reactions, the Marshall reaction and Breit's substitution, as well as the Nozaki–Hiyama–Kishi and Negishi–Fu C–C coupling reactions.

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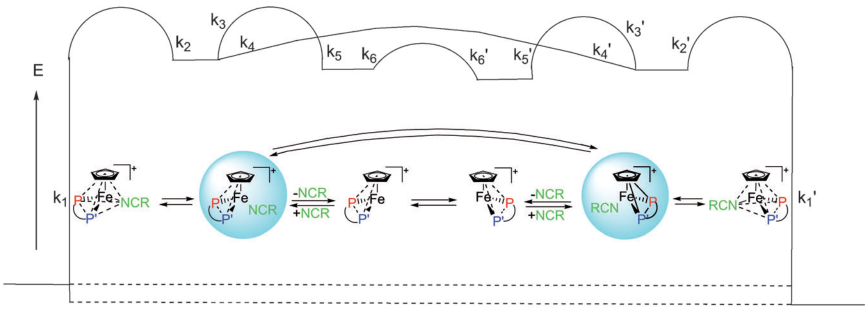
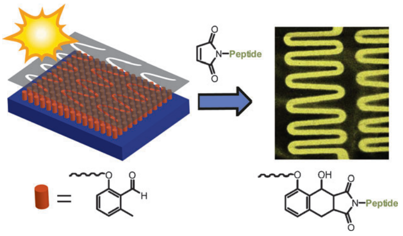
Cage Effect



Change before exchange: Cross-over experiments with chiral half-sandwich complexes [Cp′Fe(Prophos)NCR]X ($Cp' = C_5H_5$, $^{Me}C_5H_4$; X = I, PF_6), in which change of configuration at the metal atom and RCN ligand exchange compete, show that the change of the Fe configuration within the solvent cage is faster than ligand exchange (see scheme).

Clickable Surfaces

A photoconjugation strategy based on light-triggered Diels–Alder addition of *o*-quinodimethanes is compatible with biomolecules and proceeds rapidly at ambient temperature without the need of a catalyst. Spatial control was confirmed by photopatterning of a small-molecule ATRP initiator, a polymer, and a peptide in a time-of-flight secondary-ion mass spectrometry investigation.



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