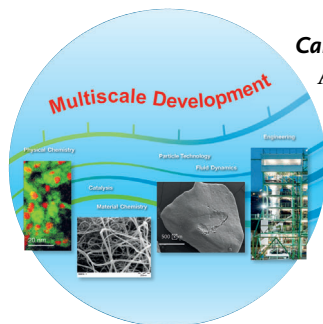




... in the fields of healthcare, crop science, and material science formed the basis of the 150 years of sustained growth at Bayer and will guarantee its future success. Recent examples such as Riociguat, a soluble guanylate cyclase (sGC) stimulator for the treatment of pulmonary hypertension, novel selective insecticidally active nicotinic acetyl choline receptor (nAChR) ligands as current and future effective agents for invertebrate pest control, as well as innovative, diverse, and versatile polyurethane-based materials, and their broad and valuable applications demonstrate Bayer's high innovation potential. The three Reviews covering these topics by M. Follmann et al. on page 9442 ff., P. Jeschke et al. on page 9464 ff., and H.-W. Engels et al. on page 9422 ff., as well as four Minireviews on carbon nanotubes, herbicides, sulfoximine pharmacophores, and electroactive polymers, written by Bayer researchers, can be found in this "150 years Bayer" issue. Many other contributions in this "150 years Bayer" issue are an indication of the worldwide collaboration between Bayer researchers and academic laboratories.



Carbon Nanotubes

As discussed by L. Mleczko and G. Lolli in their Minireview on page 9372 ff., industrial carbon nanotube production is a good example of multi-scale development, an interdisciplinary approach in which problems occurring at different scales have to be solved simultaneously.

N-H Bond Activation

H. Schwarz and co-workers show in their Communication on page 9513 ff. that both the single and double N-H bond activation of ammonia occur if $[Al_2O_3]^+$ is placed in ammonia. Mass spectrometric and theoretical investigations confirm these results.



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"... Without science, that is, without research and development, the current global challenges will not be met. Innovation safeguards the future, and not just of companies such as Bayer, but also, in more global terms, of the planet's entire population. But there are prerequisites for innovation: It is not just a question of money, but is only possible if people have the necessary ideas and passion. Innovation requires curiosity along with an enthusiasm for change and continuous improvement ..."
Read more in the Editorial by Wolfgang Plischke.

Editorial

W. Plischke ————— 9335 – 9336

150 Years of Bayer: Success through
Science-Based Innovation

Spotlight on Angewandte's Sister Journals

Service

9352 – 9355



"I like refereeing because I learn a lot of new and interesting chemistry. The biggest problem that scientists face is distraction by trivial things. ..."
This and more about Herbert W. Roesky can be found on page 9358.

Author Profile

Herbert W. Roesky ————— 9356 – 9357

The Portable Chemist's Consultant

Yoshihiro Ishihara, Ana Montero, Phil S. Baran

Books

reviewed by R. Webster,* H. Teller,
T. Kraemer ————— 9358

Essays

History of Science

M. Quack* ————— 9362–9370

Error and Discovery:
Why Repeating Can Be New



E. Fermi

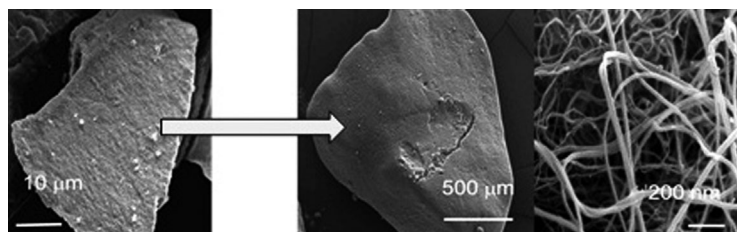
The fascinating story of the discovery of nuclear fission began with an error that earned Enrico Fermi (see picture) a Nobel Prize for the apparent but incorrect discovery of the transuranic elements. Careful repetition and extension of the experiments finally led to the correct interpretation by Hahn, Meitner, Strassmann, Frisch, and Bohr as an effect from nuclear fission of the “small impurity” of $^{235}_{92}\text{U}$ (0.7%) contained in natural uranium.

Minireviews

Carbon Nanotubes

L. Mleczko,* G. Lolli ————— 9372–9387

Carbon Nanotubes: An Example of Multiscale Development—A Mechanistic View from the Subnanometer to the Meter Scale



The scale of the problem: The catalytic synthesis of multiwall carbon nanotubes (MWCNTs) is a perfect example of multiscale development and covers challenges from the nanometer to the meter scale.

Problems, methods, and solutions for each scale must be considered. The Co/Mn reference catalyst is one of the first commercially used technologies for scalable MWCNTs production.

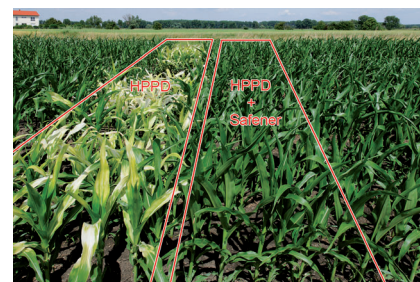
Inside Back Cover

Modern Agriculture

H. Ahrens, G. Lange, T. Müller,
C. Rosinger, L. Willms,
A. van Almsick* ————— 9388–9398

4-Hydroxyphenylpyruvate Dioxygenase Inhibitors in Combination with Safeners: Solutions for Modern and Sustainable Agriculture

Make 'em safe: Inhibitors of the HPPD enzyme prevent the formation of plant carotenoid pigments, thus resulting in the degradation of chlorophyll (see picture). Weed-control products for various crops are based on this “bleaching” mode of action. The combination with suitable safeners allows the full exploitation of the potential of herbicides to selectively control major weed problems.

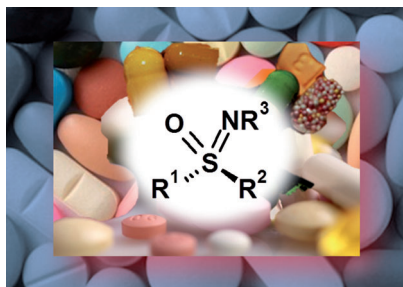


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individuals who are personal members of a national chemical society prices are available on request. Postage and handling charges included. All prices are subject to local VAT/sales tax.

The monoaza analogues of sulfones—sulfoximines—are an underrepresented pharmacophore in drug discovery approaches, even though they offer very interesting properties to the medicinal chemist. This Minireview provides an overview of the history of the sulfoximine group in medicinal chemistry, focusing on selected examples where the concept for its use as a pharmacophore and the outcome are available.



Medicinal Chemistry

U. Lücking* _____ 9399 – 9408

Sulfoximines: A Neglected Opportunity in Medicinal Chemistry



A stretch of the imagination: Electroactive polymers and especially dielectric elastomers have become more significant over the last 10 years as more applications seem possible and first products have been commercialized. The general principles of dielectric elastomers and recent developments in the field are described. The most promising developments are based on polyurethane and silicone systems. The picture shows one of the first commercial actuators based on electroactive polymers.

Dielectric Elastomers

J. Biggs, K. Danielmeier,* J. Hitzbleck, J. Krause, T. Kridl, S. Nowak, E. Orselli, X. Quan, D. Schapeler,* W. Sutherland, J. Wagner _____ 9409 – 9421

Electroactive Polymers: Developments of and Perspectives for Dielectric Elastomers



The recipe for success in polyurethane chemistry consists of the diversity of the available polymer building blocks and the resulting range of variation in material properties and applications. The challenges of our age, such as energy and resource efficiency, can be met with the outstanding durability of the fabricated products, the protection and decoration of costly articles, and as matrix materials for lightweight applications.

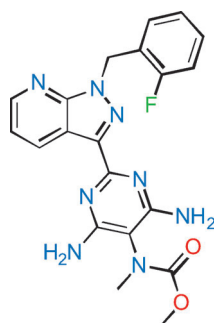
Reviews

Polyurethanes

H.-W. Engels,* H.-G. Pirkl, R. Albers, R. W. Albach, J. Krause, A. Hoffmann, H. Casselmann, J. Dormish _____ 9422 – 9441

Polyurethanes: Versatile Materials and Sustainable Problem Solvers for Today's Challenges

Front Cover



A central regulator of the circulatory system is the soluble guanylate cyclase (sGC). Two compound classes have been discovered that amplify sGC function: so-called sGC stimulators and sGC activators. Riociguat, the clinically most advanced sGC stimulator, has successfully undergone phase III trials for different forms of pulmonary hypertension and could lead to new therapies for cardiovascular disease.

Drug Discovery

M. Follmann,* N. Griebenow, M. G. Hahn, I. Hartung, F.-J. Mais, J. Mittendorf, M. Schäfer, H. Schirok, J.-P. Stasch, F. Stoll, A. Straub _____ 9442 – 9462

The Chemistry and Biology of Soluble Guanylate Cyclase Stimulators and Activators

Front Cover



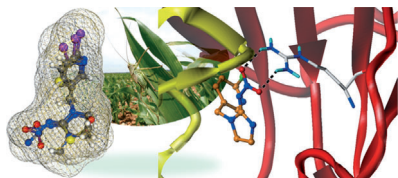
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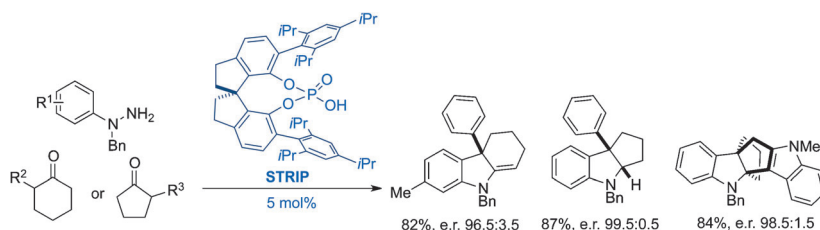
Sustainable agriculture: The discovery of neonicotinoid insecticides can be considered a milestone in crop protection research. As potent agonists selectively acting on insect nicotinic acetylcholine receptors, they also contributed to the understanding of nicotinic receptors of insects (see picture; left: superposition of various neonicotinoids; right: binding of a neonicotinoid to a receptor with an R81T mutation).

Agrochemistry/Insecticides

P. Jeschke,* R. Nauen,
M. E. Beck _____ 9464–9485

Nicotinic Acetylcholine Receptor
Agonists: A Milestone for Modern Crop
Protection

Front Cover



“Fishing” for complexity: The chiral Brønsted acid (*R*)-STRIP catalyzes the asymmetric Fischer indolization of a range of monosubstituted cyclopentanones and cyclohexanones to give chiral fused indolines bearing a quaternary stereogenic center at the 3-position. The

method has been extended to include substrates bearing a tethered nucleophile, thus allowing for enantioselective indolization/ring-closing cascades to complex propellanes featuring two vicinal quaternary stereocenters.

Communications

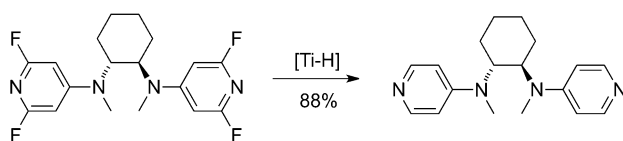
Brønsted Acid Catalysis

A. Martínez, M. J. Webber, S. Müller,
B. List* _____ 9486–9490

Versatile Access to Chiral Indolines by
Catalytic Asymmetric Fischer Indolization



Frontispiece



Fluorine makes it possible! The regioselective nucleophilic substitution of (oligo)fluoropyridines with the appropriate amines and the subsequent catalytic hydrodefluorination paves the way to hitherto inaccessible aminopyridine

derivatives, which are of interest as new ligands. Up to four fluorine atoms can be removed regioselectively in one step in a reaction employing an inexpensive titanium precatalyst.

Hydrodefluorination

G. Podolan, D. Lentz,*
H.-U. Reissig* _____ 9491–9494

Selective Catalytic Hydrodefluorination as
a Key Step for the Synthesis of Hitherto
Inaccessible Aminopyridine Derivatives

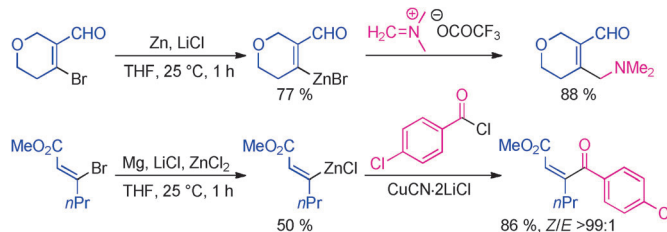


Organozinc Reagents

C. Sämann, M. A. Schade, S. Yamada,
P. Knochel* — 9495–9499



Functionalized Alkenylzinc Reagents
Bearing Carbonyl Groups: Preparation by
Direct Metal Insertion and Reaction with
Electrophiles



Highly functionalized cyclic and acyclic alkenylzinc reagents bearing functional groups such as aldehyde, keto, and ester groups were readily prepared by either direct zinc insertion in the presence of LiCl or by magnesium insertion in the

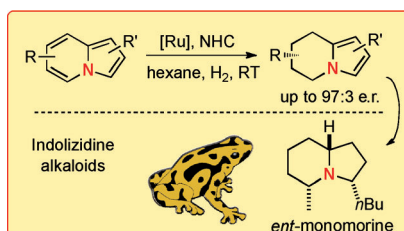
presence of LiCl and ZnCl₂. Subsequent functionalization reactions, such as Negishi cross-couplings, acylations, and allylations, furnished polyfunctional compounds in excellent yields.

Asymmetric Hydrogenation

N. Ortega, D.-T. D. Tang, S. Urban,
D. Zhao, F. Glorius* — 9500–9503



Ruthenium–NHC-Catalyzed Asymmetric
Hydrogenation of Indolizines: Access to
Indolizidine Alkaloids



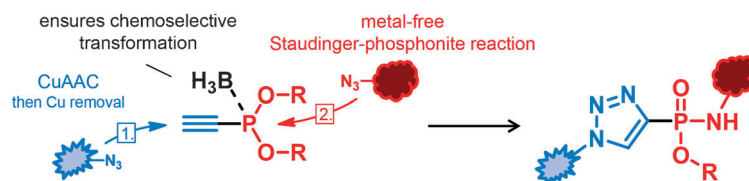
Crossing N-bridges! A ruthenium/N-heterocyclic carbene (NHC) complex serves as the catalyst for the high-yielding and completely regioselective and asymmetric hydrogenation of substituted indolizines and 1,2,3-triazolo-[1,5-*a*]pyridines. This method should provide ready access to bicyclic products bearing an N-bridgehead, a motif appearing in 25–30% of all naturally occurring alkaloids.

Azide Conjugation

M. R. J. Vallée, L. M. Artner, J. Darnedde,*
C. P. R. Hackenberger* — 9504–9508



Alkyne Phosphonites for Sequential
Azide–Azide Couplings



When Staudinger meets Huisgen! A combination of the copper-catalyzed variant of the Huisgen azide–alkyne cycloaddition (CuAAC) and the Staudinger reaction, the two most successful chemoselective reactions for the transformation of azides, leads to a chemical

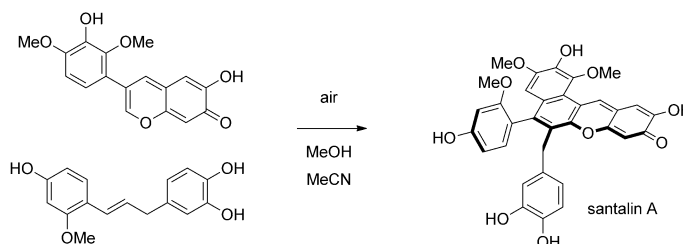
method that allows the sequential coupling of two different azido building blocks in high yields. This modular procedure enables a final metal-free conjugation of functional building blocks to azides.

Biomimetic Synthesis

S. Strych, D. Trauner* — 9509–9512

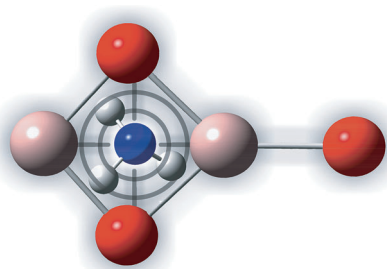


Biomimetic Synthesis of Santalin A,B and
Santarubin A,B, the Major Colorants of
Red Sandalwood



Better late than never! Almost 200 years after Pelletier's pioneering studies on the chemical constituents of red sandalwood, the major santalins and santarubins have been synthesized. This efficient approach integrates a Knochel isoflavonoid synthe-

sis with Friedel–Crafts allylations or olefin metatheses, and a final biomimetic reaction cascade that furnishes the venerable benzoxanthone dyes in a single operation (see scheme).



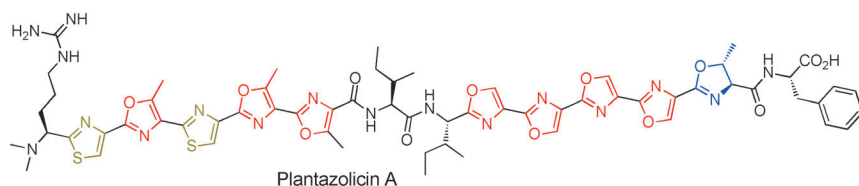
Crime scene: N–H bond activation. When ammonia gets in the crosshairs of $[\text{Al}_2\text{O}_3]^+$, the reaction is not limited to a single hydrogen-atom transfer, double hydrogen abstraction takes place as well and free nitrene is liberated at room temperature. These results are confirmed by mass spectrometric and theoretical investigations.

Radical Chemistry

R. Kretschmer, Z.-C. Wang, M. Schlangen, H. Schwarz* 9513–9517

Single and Double N–H Bond Activation of Ammonia by $[\text{Al}_2\text{O}_3]^+$: Room Temperature Formation of the Aminyl Radical and Nitrene

Back Cover



A cyclodehydration reaction has been used to synthesize the linear azole-containing peptide plantazolicin A. The target compound was synthesized from two heterocyclic fragments derived from di-

peptide building blocks. The acid-labile oxazolines and thiazoles necessitate the use of a Teoc/TMSE-based protection-group strategy, which allows structure modification of plantazolicin.

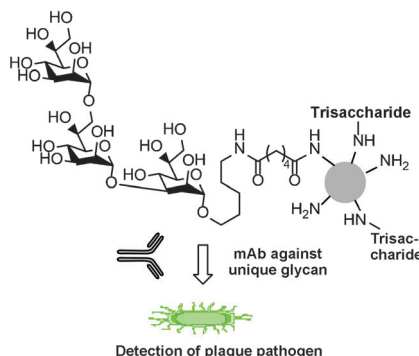
Total Synthesis

S. Banala, P. Ensle, R. D. Süssmuth* 9518–9523

Total Synthesis of the Ribosomally Synthesized Linear Azole-Containing Peptide Plantazolicin A from *Bacillus amyloliquefaciens*



The sugar coat of “Black Death” betrays it. The plague can be detected by monoclonal anti-carbohydrate antibodies. In a new technique, a plague-specific oligosaccharide antigen (see structure) is synthesized. With the help of lipopolysaccharide (LPS)-specific monoclonal antibodies (mAbs), the presence of the plague pathogen *Yersinia pestis* can then be detected in serum from patients by using a glycan microarray.



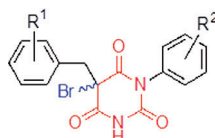
Pathogen Detection

C. Anish, X. Guo, A. Wahlbrink, P. H. Seeberger* 9524–9528

Plague Detection by Anti-carbohydrate Antibodies



The covalent grip: A new class of 5-bromobarbiturates (Cyplecksins; see structure) act by a covalent mechanism to inhibit the biological function of the pleckstrin homology domain of cytohesins, small guanine nucleotide exchange factors for the Ras-like ARF-GTPases. In cells, Cyplecksins interfere with the phosphoinositol-dependent membrane recruitment of cytohesins. Cyplecksins may be useful in validating cytohesins as potential drug targets.



Inhibitors

M. Hussein, M. Bettio, A. Schmitz, J. S. Hannam, J. Theis, G. Mayer, S. Dosa, M. Gütschow, M. Famulok* 9529–9533

Cyplecksins Are Covalent Inhibitors of the Pleckstrin Homology Domain of Cytohesin

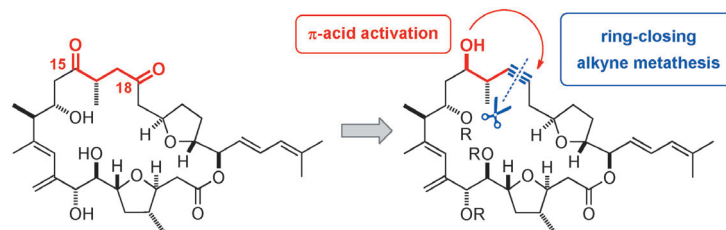


Natural Products

G. Valot, C. S. Regens, D. P. O'Malley,
E. Godineau, H. Takikawa,
A. Fürstner* ————— 9534–9538



Total Synthesis of Amphidinolide F



Orchestrated yet nonconsonant: The challenge posed by the “umposed” 1,4-dioxygenation pattern characteristic for the polyketide frame of amphidinolide F was mastered by a late-stage ring-closing alkyne metathesis followed by a directed

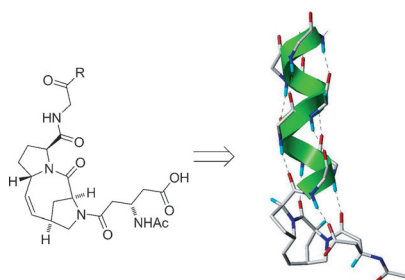
transannular hydration under the aegis of a carbophilic π -acid catalyst. This concordant strategy enabled a concise total synthesis of this enticing marine natural product.

Peptide Structure

V. Hack, C. Reuter, R. Opitz, P. Schmieder,
M. Beyermann, J.-M. Neudörfl, R. Kühne,*
H.-G. Schmalz* ————— 9539–9543



Efficient α -Helix Induction in a Linear Peptide Chain by N-Capping with a Bridged-tricyclic Diproline Analogue



Secondary structure induction: The synthetic tricyclic amino acid ProM-5, which is formally created by stereoselective introduction of a vinylidene bridge into a di-proline unit, acts as a powerful scaffold to nucleate α -helix formation in a linear peptide chain. This might be exploited in the development of new proteomimetics for the modulation of protein interactions.

DNA-Templated Chemistry

G. Li, Y. Liu, Y. Liu, L. Chen, S. Wu, Y. Liu,
X. Li* ————— 9544–9549



Photoaffinity Labeling of Small-Molecule-Binding Proteins by DNA-Templated Chemistry



DNA-templated affinity labeling: Accurate characterization of small-molecule (SM)–protein interactions is one of the most important but also very challenging tasks in chemical biology and drug discovery. A

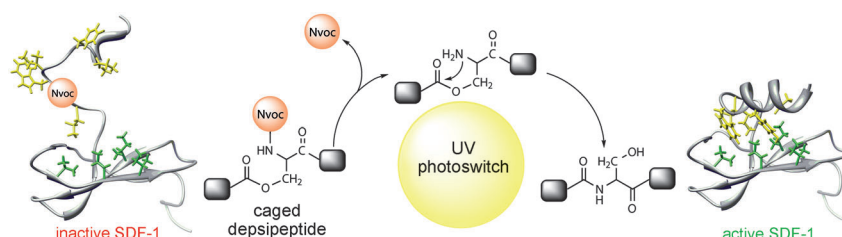
novel method named DNA-programmed photoaffinity labeling is reported. The introduction of DNA encoding and template effect enable multiplexed protein labeling by multiple probes.

Protein Engineering

L. Baumann,
A. G. Beck-Sickinger* ————— 9550–9553

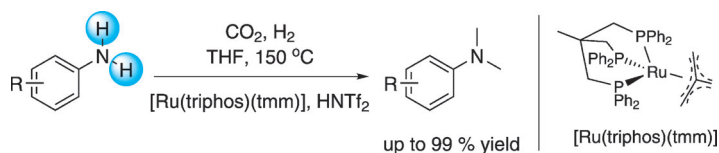


Photoactivatable Chemokines – Controlling Protein Activity by Light



Activation by light: Caged depsipeptides are incorporated as photoresponsive elements into the backbone of the protein SDF-1 α by using expressed protein ligation. The disturbed secondary structure is

restored after UV treatment by an O \rightarrow N acyl rearrangement, and the chemotactic potential of the protein is regained. Nvoc = 6-nitroveratryloxycarbonyl.



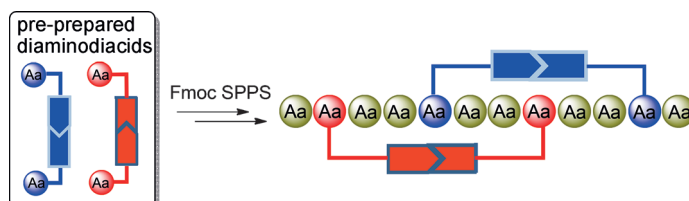
The effective catalytic N-methylation of anilines using CO_2 as C_1 source and molecular hydrogen as reducing agent was demonstrated using the well-defined $[\text{Ru}(\text{triphos})(\text{tmm})]$ catalyst. Secondary and primary (shown) aromatic amines

were mono- or dialkylated, respectively, in high yields. N-methylation of amides coupled with the amide hydrogenation offers an efficient approach to unsymmetrical tertiary methyl/alkyl/aromatic amines.

CO_2 Utilization

K. Beydoun, T. vom Stein,
J. Klankermayer,* W. Leitner **9554–9557**

Ruthenium-Catalyzed Direct Methylation of Primary and Secondary Aromatic Amines Using Carbon Dioxide and Molecular Hydrogen



The antimicrobial peptide tachyplesin I was used as a model to apply the title strategy, which was developed for the preparation of peptidic macrocycles with double disulfide surrogates. The folding and activity of the tachyplesin I analogues

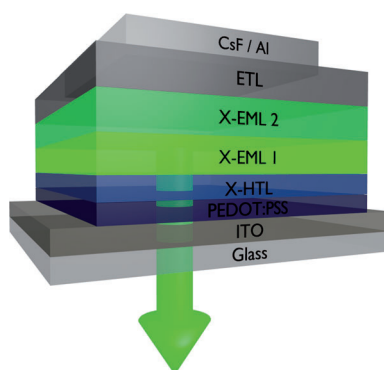
were found to be sensitive to the structure of the disulfide surrogates, thus underlining the necessity of a flexible synthetic route for generating disulfide bond surrogates with high structural diversity.

Cyclic Peptides

H.-K. Cui, Y. Guo, Y. He, F.-L. Wang,
H.-N. Chang, Y.-J. Wang, F. M. Wu,
C.-L. Tian,* L. Liu* **9558–9562**

Diaminodiacid-Based Solid-Phase Synthesis of Peptide Disulfide Bond Mimics

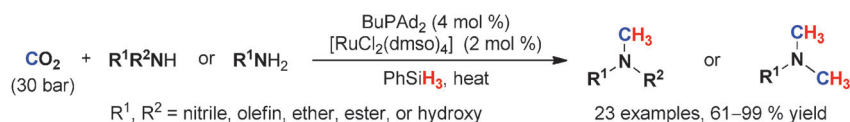
Stacks of potential: A cross-linkable host-guest system for state-of-the-art multi-layer device stacks is developed. The spirobifluorene-based host materials were co-cross-linked with green emitting phosphorescent (*fac*)- Ir^{III} complexes. As a result a five-layered organic light-emitting diode (OLED) could be fabricated in which each organic layer has been deposited from solution.



OLEDs

G. Liaptsis, D. Hertel,
K. Meerholz* **9563–9567**

Solution Processed Organic Double Light-Emitting Layer Diode Based on Cross-Linkable Small Molecular Systems



Putting CO_2 to work: Carbon dioxide is shown to be a general and selective methylating reagent for secondary and primary, aromatic and aliphatic amines under reductive conditions. A variety of

tertiary amines are obtained from CO_2 and commercially available silanes in high yields with good tolerance to nitrile, olefin, ether, ester, and hydroxy groups.

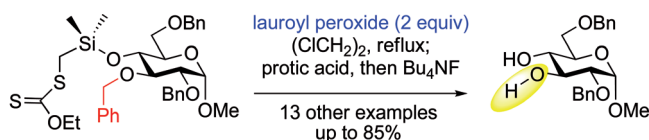
Homogeneous Catalysis

Y. Li, X. Fang, K. Junge,
M. Beller* **9568–9571**

A General Catalytic Methylation of Amines Using Carbon Dioxide

Hydrogen Transfer

A. Attouche, D. Urban,*
J.-M. Beau* 9572–9575



A Tin-Free Regioselective Radical De-O-benzylation by an Intramolecular Hydrogen Atom Transfer on Carbohydrate Templates

Radically selective: A remarkable 1,7-hydrogen atom transfer of a benzylic hydrogen atom to an O-silylmethylene radical initiates a regioselective de-O-benzylation of benzylated saccharides.

The reaction terminates by an ionic mechanism and is general for hydroxy benzylated substrates having a variety of functional groups.



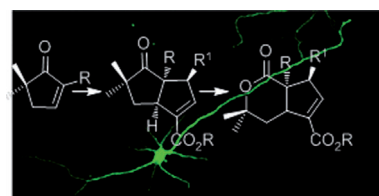
Neuritogenic Small Molecules

P.-Y. Dakas, J. A. Parga, S. Höing,
H. R. Schöler, J. Sternecker, K. Kumar,*
H. Waldmann* 9576–9581



Discovery of Neuritogenic Compound Classes Inspired by Natural Products

Neuroactive! An enantioselective, catalytic synthesis strategy provides rapid access to natural-product-inspired classes of neuritogenic compounds (see scheme). The goal is to find interesting chemical probes to shed light on neurodevelopmental processes and foster a better understanding of the complex biology and physiology of neuronal development and related neurodegenerative disorders.



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).



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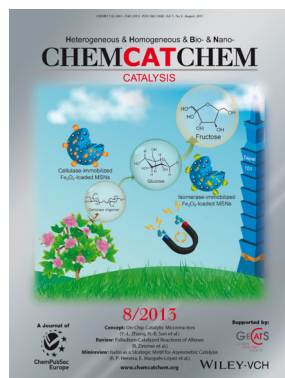


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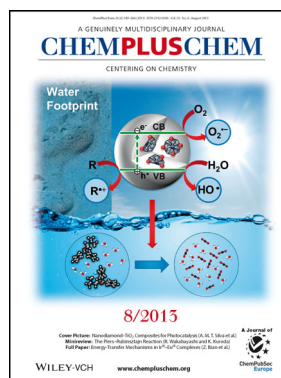
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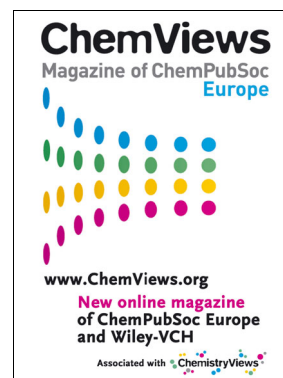
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