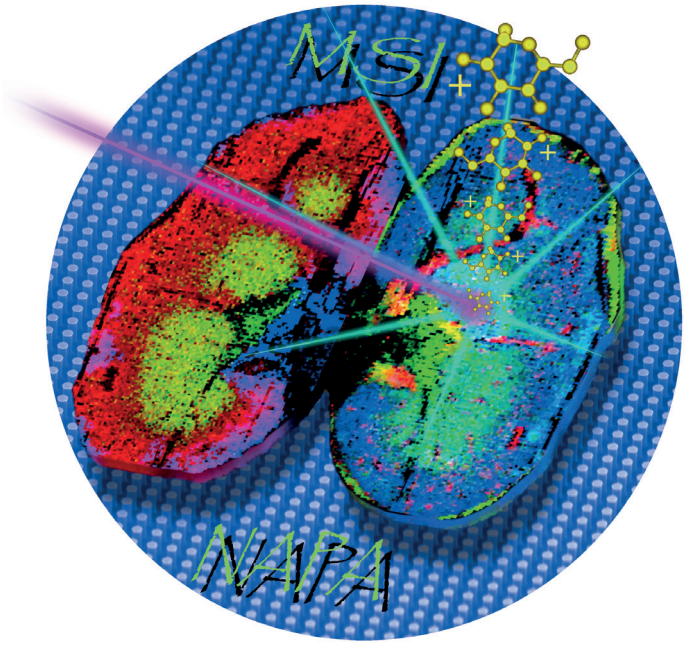
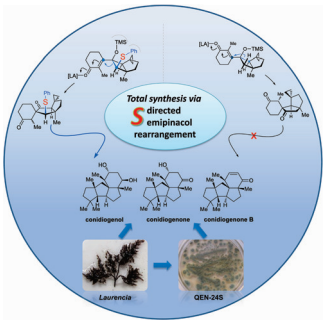
Angewandte International Edition Chemie

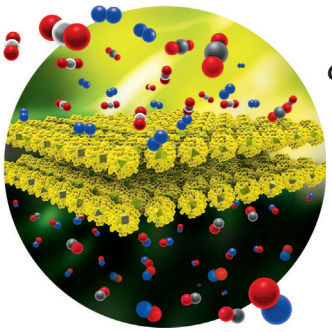


... by mass spectrometry is achieved by using nanostructured substrates. In their Communication on page 4482 ff., A. Vertes and co-workers show how laser desorption ionization from silicon nanopost arrays (NAPA) unlocks the metabolite and lipid distributions in biological tissues. The picture shows the laser pulse interacting with a mouse kidney tissue section and the underlying nanostructure to produce ions for mass spectrometry imaging (MSI).

Total Synthesis

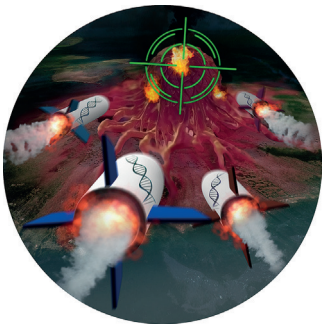
By installing a SPh "directing" group on the expected migratory carbon of the precursor, Y.-Q. Tu and co-workers in their Communication on page 4456 ff. perform the first total synthesis of cyclopiane class tetracyclic diterpenes.





Core–Shell Nanoparticles

In their Communication on page 4542 ff., H. J. Zhang, R. Jin, S. Song, and co-workers employ the biomolecule L-arginine to obtain high-quality $Pd@CeO_2$ core@shell nanocomposites with tunable Pd core sizes and shapes.



Drug Delivery

J.-H. Choy et al. report an inorganic layered double hydroxide nanovector with a folic acid conjugated surface that showed siRNA-based cancer therapeutic efficacy in their Communication on page 4582 ff.

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GDCh
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Editorial

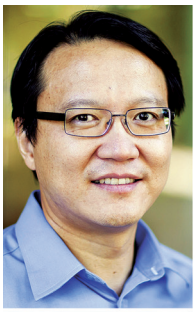
" ... The creation of robust biocatalysts with desired properties was previously challenging. Nowadays, knowledge of bioinformatics, protein engineering, molecular biology, high-throughput screening, as well as experience in biocatalysis and organic synthesis, are key skills to identify, develop, and implement novel synthetic routes ..."
Read more in the Editorial by Uwe T. Bornscheuer.

Service

Author Profile

"My favorite author (fiction) is Louis Paul Boon. The downside of my job is spending too much time away from home ..."
This and more about Geert-Jan Boons can be found on page 4392.

News



C. Yu

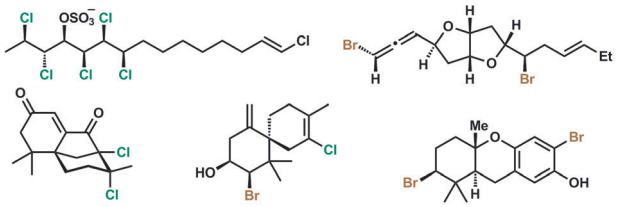
J. G. Shapter

C. J. Jackson

M. G. Kanatzidis

Reviews

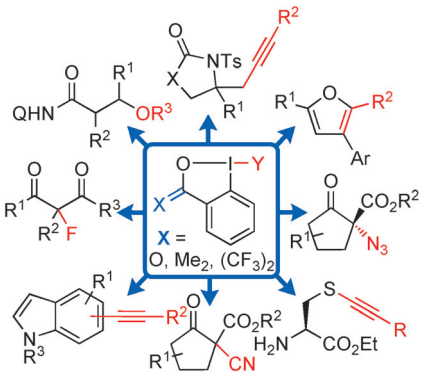
Synthetic Methods



With thousands of natural products containing halogen-bearing stereogenic centers, a wealth of methods have been developed for their stereocontrolled introduction in the context of total synthesis. This Review highlights the creative ways in which organic chemists have dealt with the challenges of stereochemically rich, halogenated natural products.

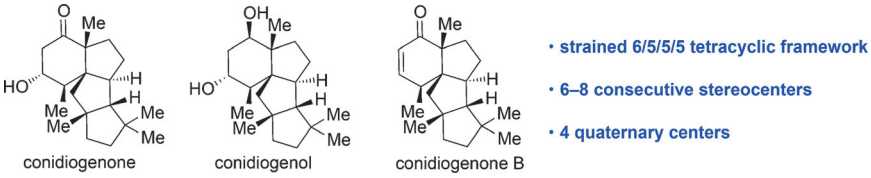
Hypervalent Iodine Compounds

The exceptional reactivity of hypervalent iodine compounds make them privileged reagents in organic synthesis. Of them, cyclic derivatives stand apart because of their enhanced stability. The use of benziodoxol(on)es for trifluoromethylation (Togni's reagents) is now well recognized, but other transformations have also attracted strong interest recently. The progress in the area since 2011 is presented in this Review. Q = 8-aminoquinoline.



Communications

Natural Products Synthesis



Three of a kind: The biologically important tetracyclic diterpenes conidiogenone, conidiogenol, and conidiogenone B (see scheme) were constructed by an efficient strategy involving an intramolecular [2+2] cyclization, a regio- and diastereoselective semipinacol rearrangement, and an intramolecular aldol cyclization as key steps. The synthesis also enabled the correction of the absolute configuration of naturally occurring conidiogenone B.

For the USA and Canada:
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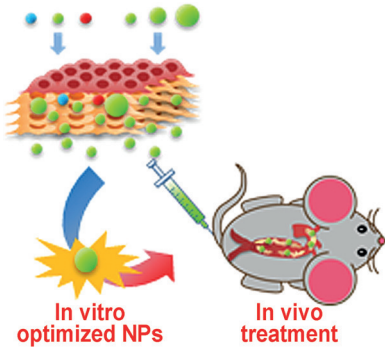
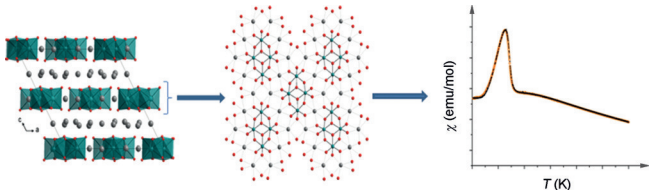


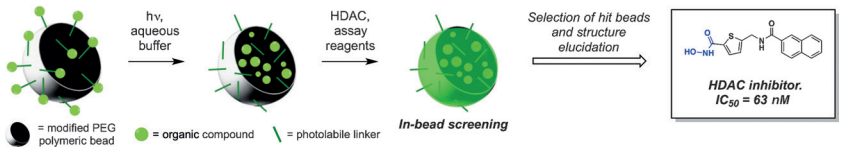
Throw away the crystal ball: Three-dimensional human-artery models allowed in vitro prediction of the in vivo behavior of drug-delivery nanoparticles. In vivo experiments with atherosclerotic mice suggested strong biological characteristics and potential treatment effects of nanoparticles optimized in vitro (see picture). This approach is a promising alternative to animal experiments for the optimization of nanomaterials.

Nanomaterials



Magnetic attraction: β-Ag_3RuO_4 was synthesized using hydrothermal conditions. The crystal structure is based on a hexagonal close packing of oxygen, and displays tetrameric polyoxoanions $[Ru_4O_{16}]^{12-}$ embedded in a 2D trigonal environment. The Ru_4 diamonds are separated by silver, which suppress the frustrated antiferromagnetic exchange common to trigonal lattices. Strong interanionic antiferromagnetic interactions dominate instead. Key: Ag gray, Ru cyan, O red.

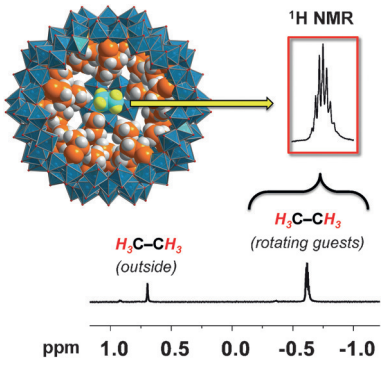
Antiferromagnetic Materials



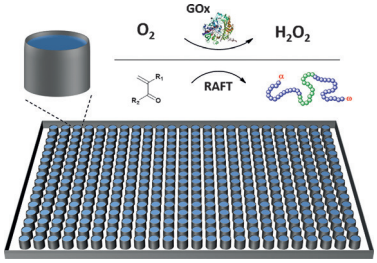
In-bead screening: A one bead–one compound screening format was developed. A combinatorial library of 55 800 hydroxamic acids were synthesized and readily screened inside polymer beads, which led to the discovery of potent HDAC inhibitors with IC_{50} values in the nanomolar range.

Drug Discovery

In the porous metal oxide capsule $[\{Mo^{VI}_6O_{21}(H_2O)_6\}_{12}\{(Mo^{V}_2O_4)_{30}(L)_{29}(H_2O)_2\}]^{41-}$ (L = propionate), the ethyl tails of the endohedrally coordinated ligands form a spherical, hydrophobic shell, while their methyl end groups generate a hydrophobic cavity at the center of the capsule. Whereas C_7 to C_3 alkanes are tightly intercalated between the ethyl tails, two or three rapidly rotating ethane molecules reside in the central cavity.

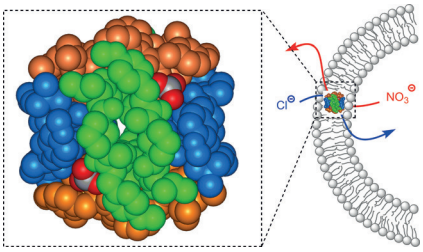


Porous Capsules

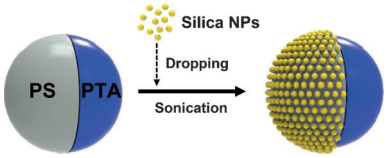


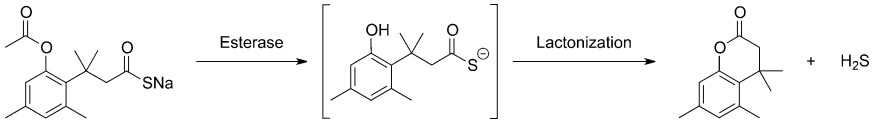
Micro-RAFTing: By using the enzyme glucose oxidase to effectively remove oxygen, highly controlled polymers are prepared in low volumes under ambient conditions on 384 well plates. This method enables the combinatorial synthesis of polymer libraries for high-throughput screening applications. RAFT = reversible addition–fragmentation chain transfer.

A cyclic octapeptide has been shown to fold into a "V-shaped" conformation that allows the selective recognition of anions such as chloride, nitrate, and carbonate. The selective anion recognition process involves the simultaneous assembly of six cyclic peptide subunits and four anions to give a supramolecular cluster that efficiently facilitates transmembrane transport of the anions.



Colloidal anisotropies: Bicompartmentalized Janus microparticles were synthesized using seeded polymerization. Selectively patching the silica nanoparticles onto one of the bulb surfaces allowed the Janus particles to assemble at the oil–water interface with a designated level of adhesion, thus producing structurally stable Pickering emulsions.





Tunable H_2S supply: Prodrugs that release hydrogen sulfide upon esterase-mediated cleavage of an ester group followed by lactonization are described (see example). By modifying the ester group and thus its susceptibility to esterase H_2S release rates can be tuned. The anti-inflammatory effects of one candidate were examined by studying its ability to inhibit TNF-α production in RAW 264.7 cells.

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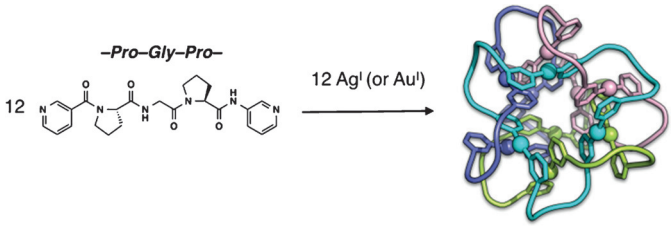
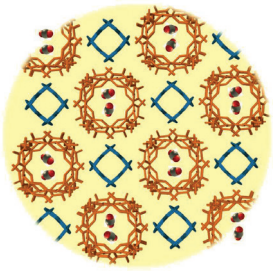
Macrocycles



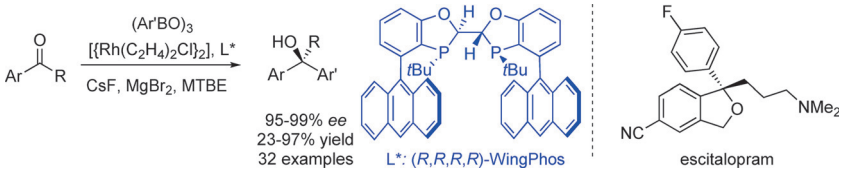
It's all about topology: Upon complexation with silver(I) the tripeptide ligand (Pro-Gly-Pro) simultaneously folds into an Ω-looped conformation and self-assembles into a discrete peptide [4]catenane with the crossing number of 12. Within the [4]catenane each of the four equivalent M_3L_3 macrocycles is interlocked with the other three rings with tetrahedral symmetry.

CO_2 Adsorption



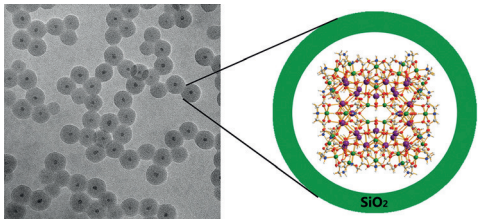
SOFly, SOFly: Two supramolecular organic frameworks (SOFs) based on *C*-pentylpyrogallol[4]arene (PgC_5) with spacer molecules, such as 4,4′-bipyridine, are prepared. Their highly optimized and symmetric intermolecular hydrogen-bonding interactions give robust extended frameworks. One of the evacuated frameworks shows excellent affinity for carbon dioxide over other gases.

Asymmetric Catalysis

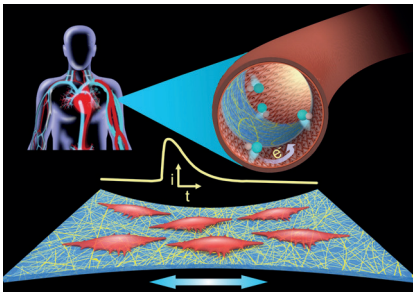


Wing it: The title reaction has been achieved for the first time with a Rh/(*R*,*R*,*R*,*R*)-WingPhos catalyst, providing a range of chiral diaryl alkyl carbinols with excellent *ee* values and yields. The method was applied for a concise synthesis of the antidepressant drug escitalopram. MTBE = *tert*-butyl methyl ether.

Magnetic Clusters



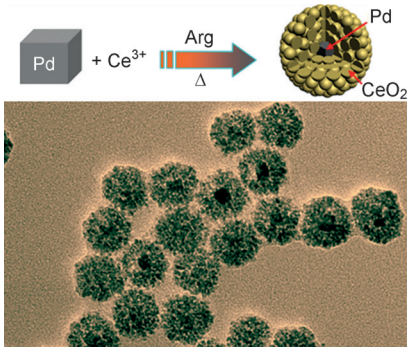
Molecular magnet: A single-molecule metal compound of **1a** encapsulated in a silica nanosphere (**1a** = $[Gd_{52}Ni_{56}(IDA)_{48}(OH)_{154}(H_2O)_{38}]^{18+}$) was prepared through a facile one-pot microemulsion method (see picture). The single-molecule high-nuclearity lanthanide–transition-metal compound showed experimentally and theoretically magnetic interactions.



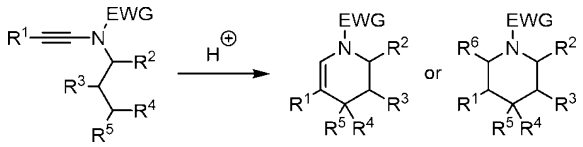
Biomedical sensor: A highly controllable strategy has been developed for synthesizing Au nanotubes with a large aspect ratio. The nanotubes were used to construct an effective stretchable electrochemical sensor and to realize real-time monitoring of mechanically sensitive cells and tissues.

Biosensors

Strictly structured: The biomolecule L-arginine triggered CeO_2 crystal growth and self-assembly on Pd nanoparticles. Following the initial formation of cerium–L-arginine precursors on the Pd surface, heat treatment led to the production of high-quality Pd/CeO_2 nanostructures (see picture). By controlling the synthetic conditions, it was possible to tune the core size and shape, nanostructure, and sheath thickness of the resulting nanospheres.

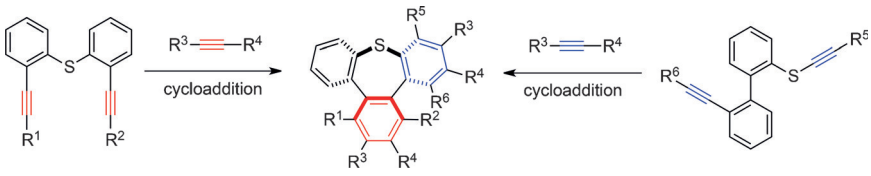


Core–Shell Nanoparticles



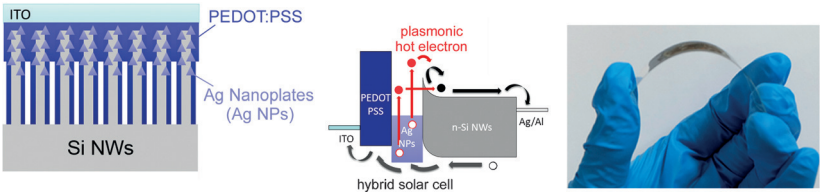
Powerful electrophiles: properly substituted keteniminium ions, simply generated by acidic treatment of the corresponding ynamides, can induce a remarkably efficient [1,5]-hydride shift from unactivated C–H bonds. This triggers a cationic cyclization which gives, within minutes, highly functionalized tetrahydropyridine and piperidine derivatives.

Heterocyclic Synthesis



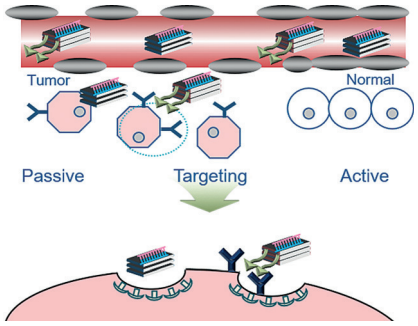
End of the tether: The first catalytic and highly enantioselective synthesis of tribenzothiepin derivatives was achieved. Two types of intermolecular cycloadditions, either using diphenyl-sulfide-tethered diynes or 2-phenyl sulfanylbenzene tethered diynes with a monoalkyne, led to chiral multisubstituted tribenzothiepins in good to excellent *ee* values under mild reaction conditions. The present protocol was used to prepare a chiral tribenzoselenepin.

Heterocycles



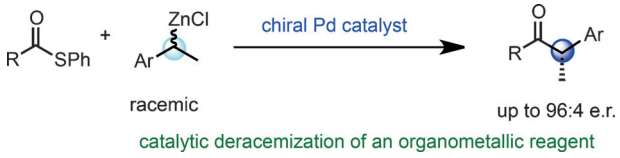
Flexible friend: The quantum efficiency of flexible photovoltaic devices in the near-infrared spectral region has been improved by integrating Si nanowire arrays with plasmonic Ag nanoplates. The Ag nanoplates can directly harvest and convert NIR light into plasmonic hot electrons for injection into Si, while the Si nanowire arrays allow light trapping. The flexible devices show excellent durability over 50 flexing cycles.

Light Harvesting



Cancer therapy: An inorganic layered double hydroxide (LDH) nanovector with a folic acid (FA) conjugated surface showed siRNA-based cancer therapeutic efficacy in vivo through receptor-mediated active targeting (see picture). A 1.2-fold higher accumulation of the drug was achieved in tumor tissue, resulting in 3.0-fold higher suppression of tumor volume.

Drug Delivery

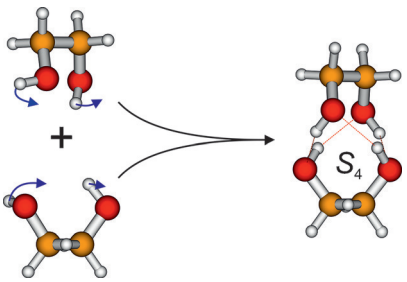


catalytic deracemization of an organometallic reagent

Converging on a moving target: The first enantioconvergent palladium-catalyzed Fukuyama cross-coupling of racemic benzylic organozinc reagents with thioesters has been developed. The reaction furnishes acyclic α,α-disubstituted ketone products in good yields and high enantioselectivities, under mild reaction conditions which prevent racemization of the potentially labile tertiary stereocenter.

Cross-Coupling

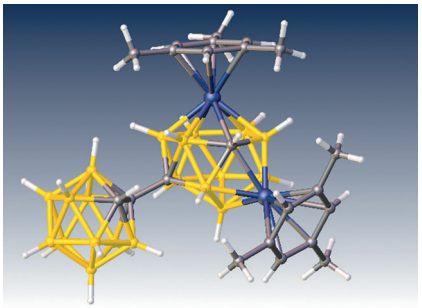
Click and lock: By twisting the OH groups in ethylene glycol, the molecule is prepared for a symmetric four-fold hydrogen-bond lock with its transient enantiomer, resulting in an outstandingly stable dimer which has so far been elusive in both theory and experiment.



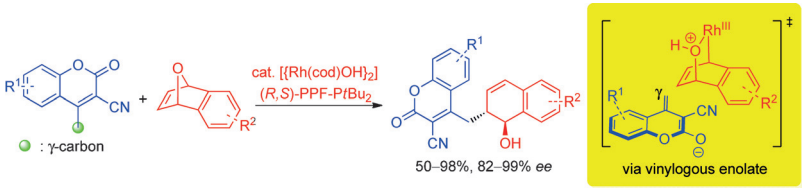
Vibrational Spectroscopy

Bis(carboranes)

Take two: Two-electron reduction of 1,1′-bis(*o*-carborane) and subsequent metalation with $\{Ru(mes)\}^{2+}$ results in a 4,1,8-RuC_2B_{10} species. A further two-electron reduction allows a direct electrophilic insertion reaction promoted by the carborane substituent for the addition of a second metal fragment and the formation of 1,13,2,9-$Ru_2C_2B_{10}$. A mechanism is proposed to rationalize the observed fluxionality of the products.

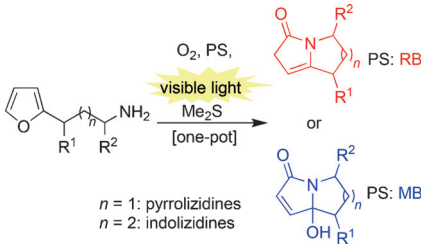


Heterocycles



Gamma style: While γ-functionalization is well established in the setting of aldol, Mannich, and Michael reactions, γ-reactivity is scarce in other reaction classes. By using the newly developed vinylogous reactivity involving the release of ring strain in the rhodium-catalyzed asymmetric ring opening (ARO) the privileged coumarin motif was incorporated into the hydronaphthalene scaffold enantioselectively.

Synthetic Methods



Singlet oxygen is able to transform unprotected primary furylalkylamines into the important pyrrolizidine and indolizidine scaffolds. The outcome of the one-pot sequences can be readily tailored to need by varying the choice of sensitizer. The synthetic utility of this method was demonstrated in the rapid synthesis of five natural products. PS: Photosensitizer. RB: rose Bengal. MB: Methylene blue.

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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