



# Swiss Science Concentrates

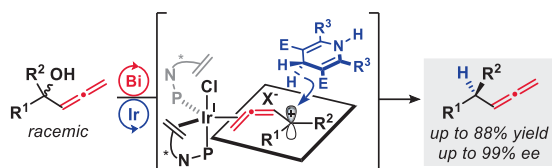
A CHIMIA Column

Short Abstracts of Interesting Recent Publications of Swiss Origin

## Coordination-Induced Stereocontrol over Carbocations: Asymmetric Reductive Deoxygenation of Racemic Tertiary Alcohols

M. Isomura, D. A. Petrone, and E. M. Carreira\*, *J. Am. Chem. Soc.* **2019**, *141*, 4738. ETH Zurich

Carreira and co-workers report a highly enantioselective reductive deoxygenation of racemic tertiary  $\alpha$ -allenyl alcohols. Their co-catalytic approach combines a chiral iridium catalyst with an achiral Lewis acid, and utilizes a novel Hantzsch ester analogue as a convenient hydride source. The allene moiety was found to be key to the success of this docking strategy, wherein coordination of an intermediate tertiary carbocation to the chiral Ir catalyst is responsible for the facial selectivity of nucleophilic attack. The authors disclosed the results of in-depth mechanistic studies which support the above mechanistic scenario which occurs after a turnover-limiting  $S_N1$ -type ionization of the allenyl C–O bond. This work constitutes the first example of asymmetric substitution of tertiary alcohols using Ir-catalysis.

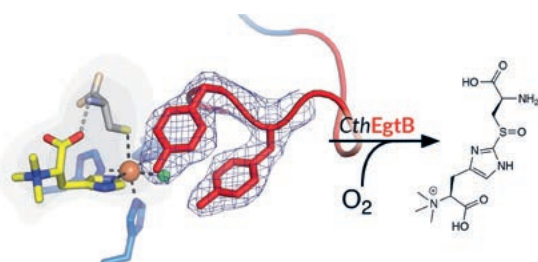


- deuterium labelling - KIE and Hammett analysis - cross-over studies -

## An Alternative Active Site Architecture for O<sub>2</sub> Activation in the Ergothioneine Biosynthetic EgtB from *Chloracidobacterium thermophilum*

A. R. Stampfli, K. V. Goncharenko, M. Meury, B. N. Dubey, T. Schirmer, and F. P. Seebeck\*, *J. Am. Chem. Soc.* **2019**, *141*, 5275. University of Basel

The complex catalytic mechanism of sulfoxide synthases, which catalyze the oxidative carbon-sulfur bond formation of cysteine derivatives and *N*- $\alpha$ -trimethylhistidine, became a controversial subject of several biochemical and computational studies. To gain further insight, Seebeck and co-workers solved the crystal structure of *CthEgtB*, which revealed a completely different configuration of active site residues than in the previously investigated *MthEgtB*. Comparison of the two structures allowed the classification of all EgtBs into five subtypes, characterized by unique active-site fea-

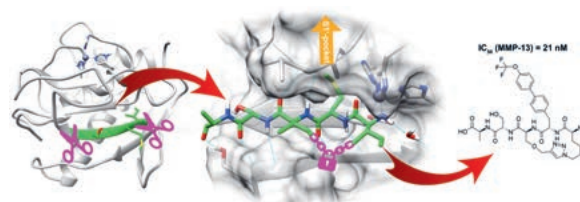


tures, hence furnishing a platform to examine the catalytic mechanism of sulfoxide synthases by comparative enzymology.

## Drug Design Inspired by Nature: Crystallographic Detection of an Auto-Tailored Protease Inhibitor Template

F. M. Gall, D. Hohl, D. Frasson, T. Wermelinger, P. R. E. Mittl, M. Sievers, and R. Riedl\*, *Angew. Chem. Int. Ed.* **2019**, *58*, 4051. University of Zurich and ZHAW Zurich University of Applied Sciences

The discovery of modulators of therapeutic targets is a challenging task. In contrast to conventional screening approaches, R. Riedl and colleagues used the therapeutically relevant proteinase MMP-13 to produce a drug against itself. They detected the partial self-degradation of the proteinase using X-ray crystallography and then converted the auto-tailored peptide ligand by structure-based de novo design into a peptidomimetic of the natural tissue inhibitors of these proteinases. Non-proteinogenic amino acids and a targeted cyclization strategy were crucial for the development of this membrane-permeable highly potent and selective MMP-13 inhibitor. This represents a new strategy for accelerating pharmaceutical drug discovery.



## Palladium-Catalyzed Intermolecular Aryliodination of Internal Alkynes

Y. H. Lee and B. Morandi\*, *Angew. Chem. Int. Ed.* **2019**, DOI: 10.1002/anie.201812396. ETH Zürich and Max-Planck Institut für Kohlenforschung

Lee and Morandi report the first Pd-catalyzed intermolecular carboiodination of alkynes to stereoselectively access functionalized tetrasubstituted iodoalkenes. The success of this reaction relies on the use of an electron-deficient bidentate ligand, dAr<sup>F</sup>pe. The method employs equimolar amounts of reactants and tolerates a broad range of functional groups. It represents an attractive alternative to previous methods employing multiple steps and requiring protecting group manipulations.

