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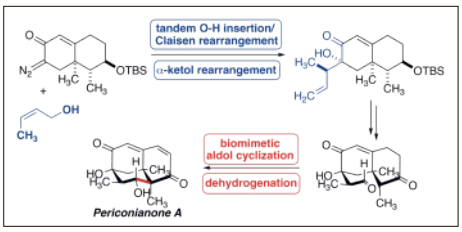
Swiss Science Concentrates

A CHIMIA Column

Short Abstracts of Interesting Recent Publications of Swiss Origin

Total Synthesis of the Periconianone A Based on a Postulated Biogenesis

Raphael Liffert, Anthony Linden, and Karl Gademann*, *J. Am. Chem. Soc.* **2017**, *139*, 16096. University of Zürich

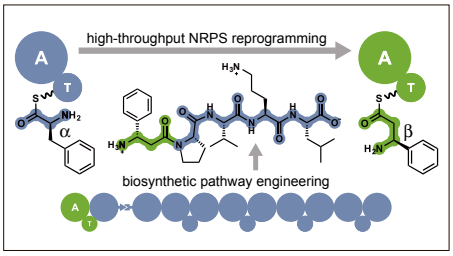


Liffert, Linden, and Gademann have successfully carried out the first total synthesis of the sesquiterpenoid periconianone A. First isolated from endophytic fungi, periconianone A possess a unique 6,6,6 carbocyclic cage-like framework that provides an interesting challenge to synthetic chemistry. The reported synthesis was inspired by a postulated biosynthetic pathway involving a late-stage aldol cyclization. Other key transformations of this total synthesis included a Criegee fragmentation and a reaction sequence involving a rhodium-catalysed hydroxy group insertion, a Claisen rearrangement and a subsequent α-ketol rearrangement. This enantioselective and concise synthesis was carried out using only one protection step, dramatically increasing the efficiency and elegance of their approach.

Nonribosomal Biosynthesis of Backbone-Modified Peptides

David L. Niquille, Douglas A. Hansen, Takahiro Mori, David Fercher, Hajo Kries, and Donald Hilvert*, *Nat. Chem.* **2017**, *10*, 282. ETH Zürich

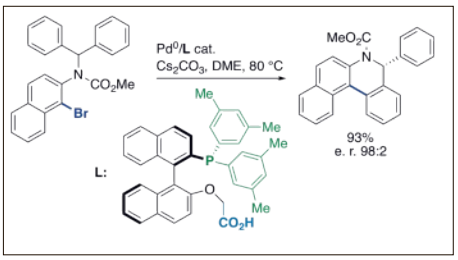
Nonribosomal peptides (NRPs) represent a class of natural products possessing unique pharmaceutical properties. The modular biosynthesis of NRPs by nonribosomal peptide synthetases (NRPSs) has inspired efforts to reprogram this mega-enzyme assembly line to access novel antibiotics. Past efforts have mostly focused on modifying amino acid side chains. In this seminal paper, The Hilvert group succeeded in changing the peptide backbone of tyrocidine by incorporating a β-amino acid, (*S*)-β-phenylalanine ((*S*)-β-Phe). Using high-throughput yeast surface display, the authors identified a variant that exhibits 40,000-fold selectivity for incorporation of the β-amino acid. The newly engineered domain was competent in the context of a complete NRPS



pathway in cells, demonstrating the feasibility of large-scale production and/or library screening of β-amino acid-containing peptides as novel therapeutics.

Chiral Bifunctional Ligands for Enantioselective C–H Arylation

Lei Yang, Markus Neuburger, and Olivier Baudoin*, *Angew. Chem. Int. Ed.* **2018**, *57*, 1394. University of Basel



Pd^0-catalyzed C-H activation reactions that proceed *via* a concerted metalation-deprotonation (CMD) mechanism provide powerful tools for constructing stereogenic centers. Yang, Neuburger and Baudoin have recently developed an efficient approach to asymmetric C–H activation using a novel binaphthyl scaffold containing both a phosphine and carboxylic acid. This bifunctional system achieved higher yields and enantioselectivities for C–H arylation as compared to the corresponding bimolecular system. This ligand was used in the first enantioselective synthesis of diverse 5,6-dihydrophenanthridines, and it enabled parallel kinetic resolution of racemic substrates. These results demonstrate the potential of bifunctional phosphine/carboxylate ligands in asymmetric C–H activation reactions involving the CMD mechanism.

Luciferases with Tuneable Emission Wavelengths

Julien Hiblot, Qiuliyang Yu, Marina D.B. Sabbadini, Luc Reymond, Lin Xue, Alberto Schena, Olivier Sallin, Nicholas Hill, Rudolf Griss, and Kai Johnsson*, *Angew. Chem. Int. Ed.* **2017**, *56*, 14556. EPF Lausanne and Max-Planck-Institute for Medical Research

Bioluminescent luciferases are widely used in reporter constructs and bioimaging. Engineered variants such as 'NanoLuc' exhibit remarkable brightness upon reacting with tailor-made substrates such as furimazine. Johnsson and co-workers developed chimeras of NanoLuc containing a SNAP-tag or HaloTag7 that exhibit efficient bioluminescence resonance energy transfer (BRET) when the SNAP/Halo tag contains a suitable, fluorescent energy acceptor *via* chemical labeling. This approach provides unprecedented access to an almost unlimited 'rainbow' of different NanoLuc emission colors that can be applied *in vitro* and *in cellulo*. This novel

class of reporter genes will provide powerful tools to diverse fields including cell biology and high-throughput drug screening.

Prepared by Aaron Johnson, Ashkan Karimi, Claire L. Lin, Verena Schreier, and Nathan W. Luedtke*

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