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Swiss Science Concentrates

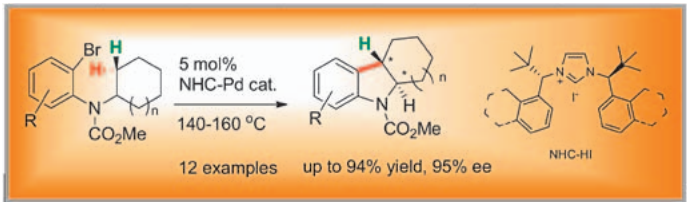
A CHIMIA Column

Short Abstracts of Interesting Recent Publications of Swiss Origin

Fused Indolines by Palladium-Catalyzed Asymmetric C–C Coupling Involving an Unactivated Methylene Group

M. Nakanishi, D. Katayev, C. Besnard, and E. P. Kündig*, *Angew. Chem. Int. Ed.* **2011**, *50*, 7438.
University of Geneva

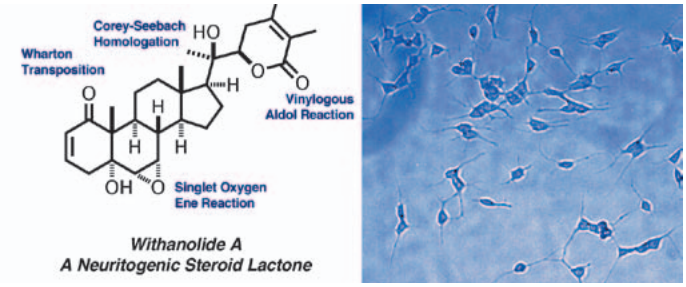
Despite the growing number of publications dealing with catalytic C(sp^3)-H activation, highly enantioselective versions of this reaction have never been reported. The authors succeed in this endeavor using either a preformed or an *in situ* generated palladium complex bearing a bulky enantiopure *N*-heterocyclic carbene ligand. The catalyst is applied in the synthesis of highly enantioenriched *trans*-fused indolines *via* a cross-coupling reaction. Remarkably, the key C–H activation step proceeds at elevated temperatures (>130 °C) with excellent asymmetric discrimination between two enantiotopic C–H bonds of an unactivated methylene unit.



Synthesis of Withanolide A, Biological Evaluation of Its Neuritogenic Properties, and Studies on Secretase Inhibition

C. K. Jana, J. Hoecker, T. M. Woods, H. J. Jessen, M. Neuburger, and K. Gademann*, *Angew. Chem. Int. Ed.* **2011**, *50,* 8407.
Department of Chemistry, University of Basel

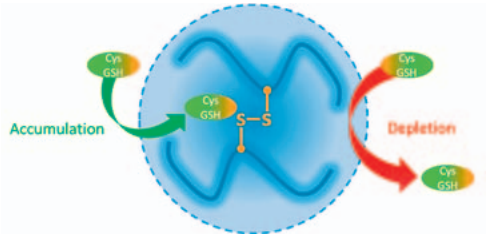
With the aging population, regeneration of neurons to treat neurodegenerative diseases is of high interest. The authors report the first stereoselective synthesis of steroid lactone whitanolide A from pregnenolone. The synthetic strategy relies on a singlet oxygen ene reaction, a vinylogous aldol reaction followed by a Wharton carbonyl transposition. With whitanolide A at hand, biological studies demonstrated neurite outgrowth. These findings support the potential neuritogenic role of this compound used in traditional Indian Ashwagandha medicine and pave the way for more detailed studies on the mechanism of action of whitanolide A.



Interplay of Chemical Microenvironment and Redox Environment on Thiol-Disulfide Exchange Kinetics

C. Wu, C. Belenda, J.-C. Leroux, and M. A. Gauthier*, *Chem. Eur. J.* **2011**, doi: 10.1002/chem.201101024.
ETH Zürich

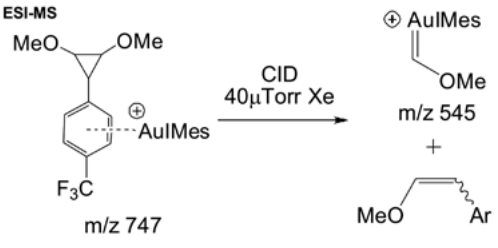
Disulfide bonds stabilize the tertiary- and quaternary structure of proteins. In addition, they can be used to engineer redox-sensitive biomaterials as well as drug-delivery systems. These applications rely on the scrambling of a disulfide bond *via* a thiol–disulfide exchange reaction, whose reaction rate is known to vary. The authors have demonstrated with a peptide scaffold that it is possible to subtly and predictably tune the rate of disulfide exchange with thiols over two to three orders of magnitude. For this purpose, they exploit electrostatic interactions. An interplay of the peptide's charge, the disulfide's microenvironment and the charge of the reducing agent leads to local accumulation or depletion of the reducing agent, which is the factor that predominately controls the rate of the reaction.



Potential Energy Surface for (Retro-) Cyclopropanation: Metathesis with a Cationic Gold Complex

A. Fedorov, L. Batiste, A. Bach, D. M. Birney, and P. Chen*, *J. Am. Chem. Soc.* **2011**, *133,* 12162.
ETH Zürich

Depending on the nature of the metal, a {M-carbene(olefin)}-moiety can lead either to cyclopropanation (*e.g.* M = Rh(II)) or to olefin metathesis (*e.g.* Ru(II)). Herein, the authors present a combined computational and experimental study of the gold-mediated cyclopropanation and metathesis reactivity of a metal-bound cyclopropane. This adduct lies in a deep minimum and fits well with the measured absolute energies of the cyclopropanation and metathesis channels. Importantly, the computed potential energy surface also accounts for the recently reported gold-catalyzed solution-phase retro-cyclopropanation reactivity.



Prepared by N. Bruns, V. Köhler, R. Kramer, P. Mauleón, F. Monnard, A. Ganic and T. R. Ward
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