



Swiss Science Concentrates

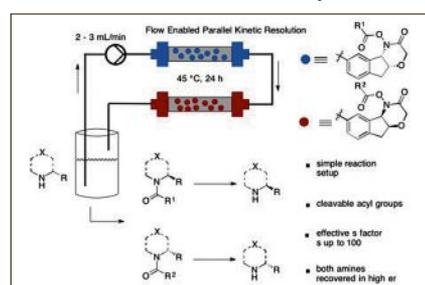
A CHIMIA Column

Short Abstracts of Interesting Recent Publications of Swiss Origin

Flow Chemistry and Polymer-supported Pseudoenantiomeric Acylating Agents Enable Parallel Kinetic Resolution of Chiral Saturated N-Heterocycles

I. Kreituss and J. W. Bode*, *Nat. Chem.* **2016**, DOI 10.1038/nchem.2681. ETH Zürich

Kinetic resolution (KR) is widely used for the separation of enantiomers. Unless reagents, such as enzymes, with very large selectivity factors are used, KR is typically not appropriate if both enantiomers are needed in high enantiopurity. Parallel kinetic resolution (PKR) – in which both enantiomers undergo reactions with pseudo-enantiomeric reagents – may provide a solution. Kreituss and Bode describe the development of a user-friendly, flow-based system that enables practical PKR of saturated N-heterocycles. Two immobilized quasi-enantiomeric acylating agents were designed for the asymmetric acylation of racemic saturated N-heterocycles. The process provided access

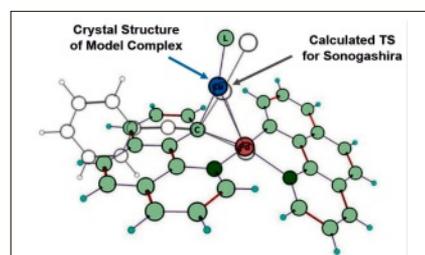


to both enantiomers in good yield and high enantiopurity. The concept should prove useful in other chemical processes that benefit from physical separation of distinct reagents or catalysts.

Structure and Gas-phase Thermochemistry of a Pd/Cu-Complex: Studies on a Model for Transmetalation Transition States

R. J. Oeschger and P. Chen*, *J. Am. Chem. Soc.* **2017**, 139, 1069. ETH Zürich

All palladium-catalyzed cross-coupling reactions follow a general catalytic cycle, in which a transmetalation reaction appears as one of the key steps. Oeschger and Chen now describe a heterobimetallic Pd(II)/Cu(I) complex that serves as a model for the transmetalation transition state. The crystal structure shows a remarkably short Pd–Cu bond and a trigonal *ipso* carbon atom. The Pd–Cu interaction models the net stabilizing energy of the Pd–Cu interaction in the transition state of the transmetalation step in Pd/Cu catalyzed cross-coupling reactions. The concept of transmetalation being

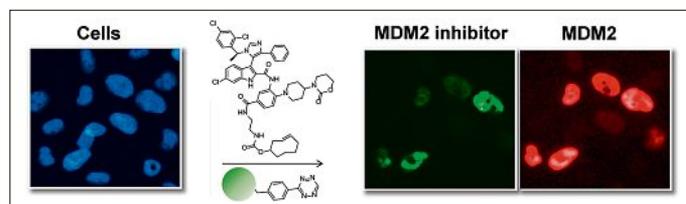


facilitated by metal–metal interactions might be applicable to other bimetallic transition metal catalyzed reactions and can potentially lead to the development of more efficient catalytic reactions.

Bioorthogonal Probes for the Study of MDM2-p53 Inhibitors in Cells and Development of High-content Screening Assays for Drug Discovery

P. L. D'Alessandro, N. Buschmann, M. Kaufmann, P. Furet, F. Baysang, R. Brunner, A. Marzinzik, T. Vorherr, T.-M. Stachyra, J. Ottl, D. E. Lizos,* and A. Cobos-Correa*, *Angew. Chem. Int. Ed.* **2016**, 128, 16260. Novartis Basel

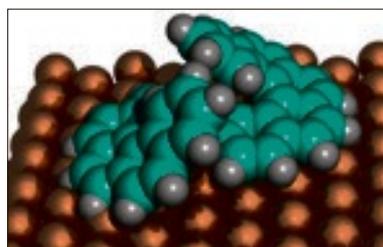
The tumor suppressor protein p53 plays a pivotal role in DNA repair, cell cycle regulation, apoptosis, angiogenesis, and senescence. To study the behaviour of MDM2-p53 inhibitors in a disease-relevant cellular model, Lizos, Cobos-Correa and collaborators developed a set of bioorthogonal probes that can be fluorescently labelled in cells and used in high-content screening assays. Automated image analysis with single-cell resolution allowed the visualization of intracellular target binding of compounds and quantification of target upregulation upon MDM2-p53 inhibition in an osteosarcoma model. The methods presented here for MDM2 should be applicable to other targets and disease models.



Heterochiral to Homochiral Transition in Pentahelicene 2D Crystallization Induced by Second-layer Nucleation

A. Mairena, L. Zoppi, J. Seibel, A. F. Tröster, K. Grenader, M. Parschau, A. Terfort, and K.-H. Ernst*, *ACS Nano* **2017**, 11, 865. Empa Dübendorf, Universität Zürich

Submolecular resolution of STM allows the discrimination of absolute configuration of single chiral molecules. Ernst and coworkers report chiral recognition phenomena in the 2D crystallization of [5]helicene on a Cu(111) surface. Homochiral, van der Waals bonded dimers form heterochiral as well as homochiral long-range ordered structures. 2D racemate crystals are observed at coverages close to a full monolayer. As the coverage leads to second-layer nucleation, the dense racemate phase in the first layer disappears and a homochiral dimer conglomerate phase



arises. The results show that at the onset of second-layer nucleation a local change of enantiomeric composition in the first layer occurs, causing there a transition from a 2D racemate to a 2D conglomerate.