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Swiss Science Concentrates

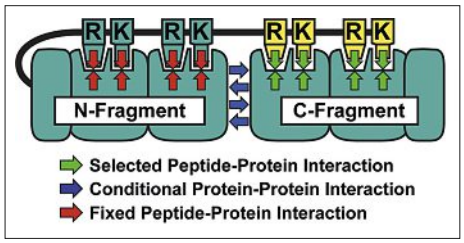
A CHIMIA Column

Short Abstracts of Interesting Recent Publications of Swiss Origin

Peptide-guided Assembly of Repeat Protein Fragments

Erich Michel*, Andreas Plückthun, and Oliver Zerbe*, *Angew. Chem. Int. Ed.* **2018**, *57*, 4576. University of Zurich

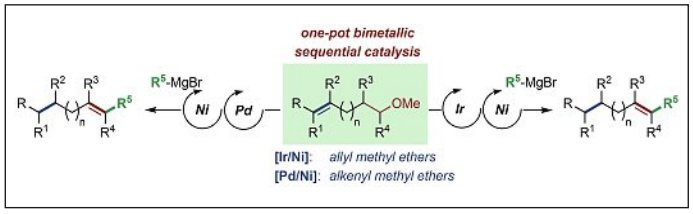
Directed evolution methods enable the creation of binders for virtually any peptide, protein, nucleic acid, and even small molecule. These procedures are typically based on the combinatorial modification of loops and/or surfaces of a protein to improve affinity towards its target. This approach is highly successful in terms of achieving high affinity, but specificity is often a limiting factor. Michel, Plückthun and Zerbe discovered a new approach using complementary fragment mixtures of designed armadillo repeat proteins (dArmRPs) that only assemble in the presence of a templating peptide and thereby facilitates enrichment of specific combinations. As little as four amino acids of the templating octapeptide were necessary to trigger formation of high-affinity complexes with K_d values in the low nM range. The selection power of this method can be harnessed to select binders of target peptides that differ by only a single residue.



Multicatalytic Synthesis of Highly Substituted Alkenes by Sequential Isomerization/Cross-Coupling Reactions

Ciro Romano and Clément Mazet*, *J. Am. Chem. Soc.* **2018**, *140*, 4743. University of Geneva.

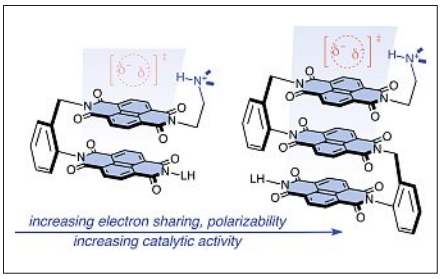
Mazet and Romano have developed a creative relay system which can interconvert two distant functional groups irrespective of the linker length separating them. Such one-pot reactions are highly sought after as they allow for the rapid increase of molecular complexity. However, these types of sequential catalytic reactions are challenging due to the difficulty in identifying highly effective, orthogonal catalytic systems. This has been achieved with iridium-catalyzed olefin migration in allyl methyl ethers to afford methyl vinyl ethers, followed by refunctionalization of the methoxy group to aryl using a nickel catalyst. The isomerization distance could be further expanded with the replacement of the iridium with a palladium-based catalyst. This approach was showcased with an olefin walk of up to nine bonds.



Synergistic Anion-$(\pi)_n$-π Catalysis on π-Stacked Foldamers

Anna-Bea Bornhof, Antonio Bauzá, Alexander Aster, Marion Pupier, Antonio Frontera, Eric Vauthey, Naomi Sakai, and Stefan Matile*, *J. Am. Chem. Soc.* **2018**, *140*, 4884. University of Geneva

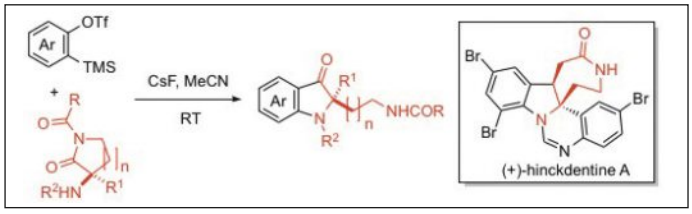
Unprecedented catalytic activity of π-stacked foldamers has been discovered by Matile and co-workers. Their approach utilized anion-π interactions on covalent oligomers of π-stacked naphthalendiimides (NDIs). The NDIs π-acidic surfaces serve as an effective catalyst for the addition of malonate half thioesters to enolate acceptors – a key biosynthetic reaction. The NDI foldamers were able to discriminate planar versus bent tautomers of the anionic malonate half thioester to facilitate catalysis. Interestingly, the expected sublinear increase in NDI surface potential with increasing number of π-stacked units was not reflected in the superlinearity observed for the increase of anion–π catalysis with increasing unit number. A key question now is where do these gains in catalytic activities with increasing length of the π stack 'top out'?



Heteroannulation of Arynes with α-Amino Imides

Rubén O. Torres-Ochoa, Thomas Buyck, Qian Wang, and Jieping Zhu*, *Angew. Chem. Int. Ed.* **2018**, *57*, 5679. EPFL Lausanne.

Zhu and co-workers developed a novel heteroannulation reaction employing aryne chemistry to synthesize α,α-disubstituted indolin-3-ones. After observing no such product formation using methyl α-amino ester, they discovered that α-amino imides were suitable starting materials to achieve this key, ring-forming reaction. The broad scope of this reaction allowed them to construct an array of derivatives with modifications carried by both the benzyne and α-amino imide components. Furthermore, they showcased this new methodology with an enantioselective total synthesis of (+)-hinckdentine A. This natural product presented an intriguing challenge, containing a unique combination of indoline, azepinone, and pyrimidine motifs in the same structure.



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

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