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A CHIMIA Column

Short Abstracts of Interesting Recent Publications of Swiss Origin

Structure of a Promiscuous Thioesterase Domain Responsible for Branching Acylation in Polyketide Biosynthesis

Amy E. Fraley,* Cora L. Dieterich, Mathijs F. J. Mabesoone, Hannah A. Minas, Roy A. Meoded, Franziska Hemmerling, and Jörn Piel*

Angew. Chem. Int. Ed. **2022**, *61*, e202206385,
<https://doi.org/10.1002/anie.202206385>

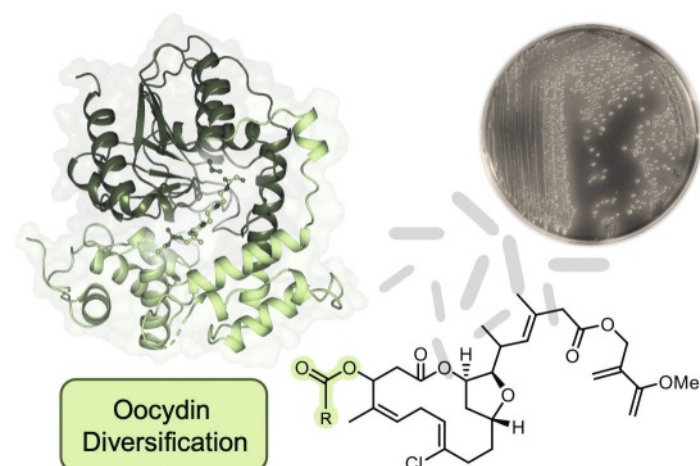
Department of Biology, Institute of Microbiology, Eidgenössische Technische Hochschule (ETH) Zurich

Oocydin-type polyketides exhibit potent anticancer, anti-oomycete, and counter-hypolipidemic bioactivity. However, some of these polyketides require acylation to either induce their activity or to increase their drug-like properties such as metabolic stability, membrane permeability, and bioavailability.

In the highlighted paper, Piel and co-workers report the structural and functional insight into the first thioesterase domain known to perform these diverse acylations in polyketide biosynthesis. Using a structure-based enzyme engineering approach they generated a versatile *O*-acyltransferase, with the potential for stereoselective synthesis of acylated polyketides. Hence, their newly engineered biocatalyst could prove a valuable synthetic biology tool for polyketide drug development.

Authors' comments:

“This work is unique because the novel enzymology ultimately led us to look back at the native host and discover a suite of previously unidentified oocycin natural product analogs.”



Towards Hexagonal Planar Nickel: A Dispersion-stabilised Tri-Lithium Nickelate

Andryj M. Borys, Lorraine A. Malaspina, Simon Grabowsky, and Eva Hevia*

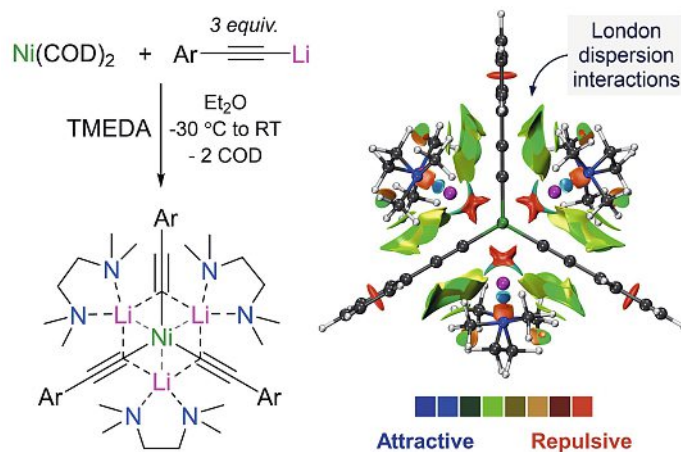
Angew. Chem. Int. Ed. **2022**, *61*, e20220979,
<https://doi.org/10.1002/anie.202209797>

University of Bern

Despite their synthetic relevance, only a few low valent lithium nickelates have been isolated and characterised. As a consequence, currently there is limited understanding on the nature of the bonding in these complexes. This work reports the successful isolation of homoleptic tri-lithium nickelates from readily available Ni(COD)₂ and lithium aryl-acetylides in the presence of bidentate donor TMEDA. Uncovering a novel structural motif, these complexes adopt a rare hexagonal planar geometry in the solid state. In depth analysis of the bonding in these complexes using a combination of QTAIM, NCI and NBO methods, revealed that the Li–Ni interactions are repulsive in nature. Contrastingly, dispersion interactions between the TMEDA donor and acetylide substituents on nickel are found to play a crucial role in the stabilisation and thus isolation of these elusive complexes.

Authors' comments:

“The complementary theoretical studies allowed us to understand the true structure and bonding of a homoleptic tri-lithium nickelate – a unique motif that was first proposed over 40 years ago.”



Mimicry of the proton wire mechanism of enzymes inside a supramolecular capsule enables β -selective O-glycosylations

Tian-Ren Li, Fabian Huck, Giovanni Maria Piccini, and Konrad Tiefenbacher*

Nat. Chem. **2022**, *14*, 985,

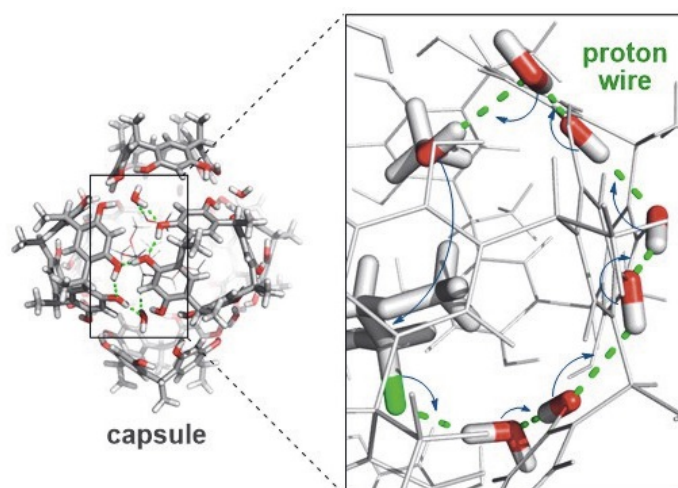
<https://doi.org/10.1038/s41557-022-00981-6>

University of Basel, ETH

Nature achieves high substrate and product selectivity by orienting and activating the substrate(s) inside a well-defined binding cavity. Mimicking such a system has been the goal of many research endeavours, albeit using simpler molecular systems. However, the use of proton wires has not been observed in man-made catalysts. They involve a dual activation of a nucleophile and an electrophile *via* a reciprocal proton transfer (see proton wire in green below) and enable highly stereoselective reactions under mild conditions. Here, the authors elegantly create said phenomena using a supramolecular resorcin[4]arene capsule. Catalytic and highly stereoselective β -glycosylations were successfully performed inside the cavity of the capsule. Moreover, this activation mode could be used on a broad scope of glycosyl donors and acceptors. Due to the ready availability of the catalyst and the excellent selectivity observed in the reported reactions, the authors believe that the methodology has high potential for broad applicability in the scientific community.

Authors' comments:

"We were really excited when we found evidence for the proton wire mechanism, as we initially expected a different activation mode for the glycosylation reaction inside the resorcin[4]arene capsule."



Two novel dinuclear cobalt polypyridyl complexes in electro- and photocatalysis for hydrogen production: cooperativity increases performance

Nicole Weder, Nora S. Grundmann, Benjamin Probst, Olivier Blacque, Rangsiman Ketkaew, Fabrizio Creazzo, Sandra Luber, and Roger Alberto*

ChemSusChem, **2022**, *15*(17), e202201049,

<https://doi.org/10.1002/cssc.202201049>

University of Zurich

Cobalt polypyridyl complexes are of ongoing interest in photocatalytic water splitting. However, their higher overpotentials compared to other molecular water reduction catalysts (WRCs) decreases the efficiency of light-induced proton reduction. While structural, spectroscopic or magnetic properties of multinuclear cobalt complexes were studied, investigations of water-reducing properties of these complexes are scarce. Herein, the authors report on the synthesis and characterization of two new, dinuclear Co-polypyridyl water reduction catalysts containing equivalent pentadentate cobalt-binding sites linked by either a bipyridyl or a pyrazyl bridge. Upon comparison with the single-core mononuclear analogue, cooperativity of the cobalt centres in the dual-core catalyst was highlighted with respect to catalytic rates and decreased overpotential. Overall, this study provides an innovative, stable and efficient cobalt polypyridyl catalyst with electronically coupled cobalt centres for the hydrogen evolution reaction.

Authors' comments:

"In-depth analysis of the electrochemical data combined with computational studies and simulations are fundamental to elucidate the hydrogen formation mechanisms and to assess the cooperation between the two cobalt centres."

