doi:10.2533/chimia.2024.349 Chimia 78 (2024) 349–350

Swiss Science Concentrates

A CHIMIA Column

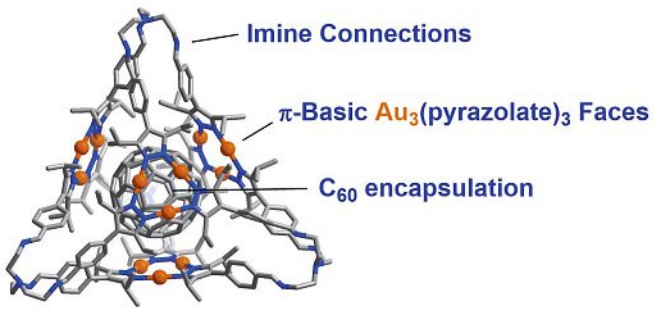
Short Abstracts of Interesting Recent Publications of Swiss Origin

Molecular Imine Cages with π-Basic Au_3(pyrazolate) Faces

Noga Eren, Farzaneh Fadei-Tirani, Rosario Scopelliti, Kay Severin,
Chem. Sci., **2024**, *15*, 3539
https://doi.org/10.1039/D3SC06280E
EPFL

This work describes the synthesis and characterization of innovative supramolecular cages containing trinuclear gold complexes, Au_3(pyrazolate)$_3$, connected *via* dynamic covalent imine chemistry. One tetrahedral and two trigonal prismatic cages with π-basic Au_3(pyrazolate)$_3$ faces are reported. The parallel arrangement of these complexes in the prismatic cages enhances interaction with π-acids, as demonstrated by the encapsulation of polyhalogenated aromatic compounds. The tetrahedral cage acts as a receptor for fullerenes, forming adducts with C_{60} and C_{70}. The structures of the cages and adducts have been established through X-ray crystallography. Unlike previous cages based on Au_3(pyrazolate)$_3$ complexes, these imine cages are soluble in chlorinated organic solvents, allowing for detailed solution-based analyses and single-crystal XRD measurements. The study highlights the potential of Au_3(pyrazolate)$_3$ complexes in molecularly defined nanostructures with interesting host-guest chemistry.

Authors' comments:
"Trinuclear Au_3(pyrazolate)$_3$ complexes exhibit significant π-basicity. Through the integration of these complexes into cage-like assemblies, it is possible to obtain compounds with unique host-guest properties."

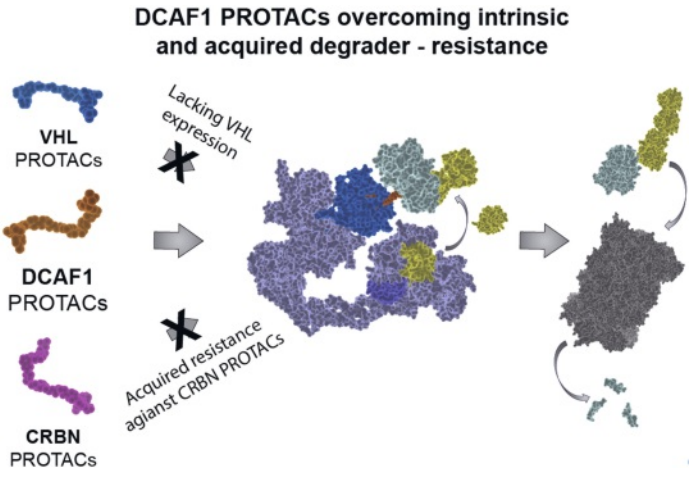


DCAF1-Based PROTACs with Activity Against Clinically Validated Targets Overcoming Intrinsic- and Acquired-Degrader Resistance

Martin Schröder, Martin Renatus, Xiaoyou Liang, Fabian Meili, Thomas Zoller, Sandrine Ferrand, Francois Gauter, Xiaoyan Li, Frederic Sigillot, Claudio R. Thoma, *et al.*
Nat. Commun. **2024**, *15*, 275.
https://doi.org/10.1038/s41467-023-44237-4
Novartis Institutes for Biomedical Research, Basel, Switzerland; Novartis Institutes for Biomedical Research, Cambridge, MA, USA; Friedrich Miescher Institute for Biomedical Research, Basel, Switzerland.

Proteolysis Targeting Chimeras (PROTACs) revolutionize drug development by redirecting E3 ligases to ubiquitinate and degrade specific proteins. Curiously, the pivotal ligase CRBN is observed to decline in scenarios of resistance to immunomodulatory inhibitory drugs (IMiDs). This study explores the potential of utilizing the E3 ligase receptor DCAF1, employing a non-covalent DCAF1 binder transformed into a PROTAC E3 ligase anchor. Validation through chemical and genetic experiments confirms specific degradation *via* the CRL4 E3 ligase. This innovative strategy could provide an alternative to overcome predicted resistance against CRBN-targeting PROTACS in clinical settings, shedding light on the promising prospect of leveraging DCAF1 for targeted protein degradation in drug development.

Authors' comments:
"The herein described DCAF1 ligands expand the spectrum of usable tool compounds to further investigate DCAF1 cellular functions and its potential as a ligase for TPD."



Prepared by Cesare Berton, Patrick A. Cieslik, Fan Liu, Simon Klinger, Jonas Genz, Ben Boback, Deborah Bäcker, Dominik Roth, Samy Kichou, Eda Nisli, Stanislav Prytuliak and Jason P. Holland*

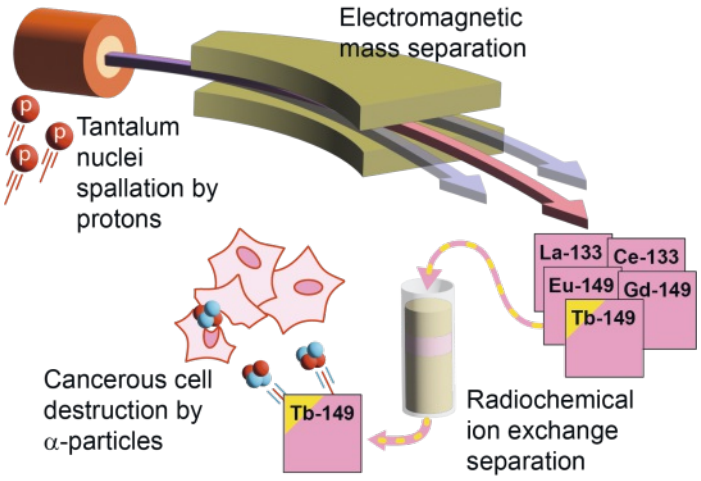
Do you want your article to appear in the SWISS SCIENCE CONCENTRATES highlight?
Please contact jason.holland@chem.uzh.ch

Terbium-149 Production: A Focus on Yield and Quality Improvement Towards Preclinical Application

Chiara Favaretto, Pascal V. Grundler, Zeynep Talip, Ulli Köster, Karl Johnston, Sarah D. Busslinger, Peter Sprung, Colin C. Hillhouse, Robert Eichler, Roger Schibli, Cristina Müller, and Nicholas P. van der Meulen*
Sci. Rep. **2024**, *14*, 3284.
https://doi.org/10.1038/s41598-024-53610-2
Paul-Scherrer-Institute, ETH Zurich

Terbium-149 ($t_{1/2}$ = 4.1 h, E_α = 3.98 MeV) is a promising radionuclide for targeted alpha therapy, offering potential benefits of reduced toxicity to healthy tissue due to minimal emission of α-emitting daughter nuclides. This study produced terbium-149 *via* 1.4 GeV proton irradiation of a tantalum target at CERN-ISOLDE. Spallation products were mass separated, implanted on zinc-coated foils, and processed. Terbium-149 was isolated from co-produced isotopes and the zinc coating using cation-exchange and extraction chromatography. Up to 260 MBq terbium-149 were obtained with >99% radionuclidic purity, achieving 50 MBq/nmol apparent molar activity in DOTATATE radiolabeling with >99% radiochemical purity. Chemical purity, assessed by inductively coupled plasma–mass spectrometry, revealed only trace levels of lead, copper, iron, and zinc. *In vivo* PET/CT scans in xenografted mice exhibited significant tumor uptake, affirming product quality for preclinical use.

Authors' comments:
"This collaborative work is the culmination of a decade's development. Beam time at CERN-ISOLDE is extremely sought after and, therefore, limited. Collection capability at ISOLDE was optimized while, in parallel, the chemical separation improved. This has resulted in products suitable for preclinical therapy studies."



Hydroamination of Triisopropylsilyl Acetylene Sulfur Pentafluoride – a Bench-top Route to Pentafluorosulfanylated Enamines

Jonas O. Wenzel, Fabian Jester, Antonio Togni, and David Rombach
Chem. Eur. J. **2023**, *63*, e202316393
https://doi.org/10.1002/chem.202304015
University of Zürich

A novel benchtop protocol introduces (triisopropylsilyl)acetylene sulfur pentafluoride (TASP) as a key reagent for accessing elusive α-SF_5 aldehyde enamines under mild conditions. This method overcomes challenges in synthesizing vinylic pentafluorosulfanylated compounds, crucial for medicinal and material sciences. TASP enables hydroamination of alkynes, demonstrating high diastereoselectivity and stability of SF_5-enamines. The protocol's simplicity, coupled with insights into the reaction mechanism, promises broader utility for SF_5-containing molecules. Additionally, TASP facilitates the synthesis of SF_5 vinyl sulfides. These breakthroughs pave the way for easier access to SF_5 motifs, eliminating the need for hazardous reagents or specialized conditions on-site.

Authors' comments:
"This reagent allows various previously undescribed pentafluorosulfanylated compounds to be made accessible to non-specialized laboratories. We hope that these methods will contribute to further research on pentafluorosulfanylated building blocks."