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Swiss Science Concentrates

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Short Abstracts of Interesting Recent Publications of Swiss Origin

Interrogating the *anti*-Insertion of Alkynes into Gold(III)

Jaime Martín, Johannes Schörgenhumer, and Cristina Nevado*

JACS Au **2025**, *5*, 1439
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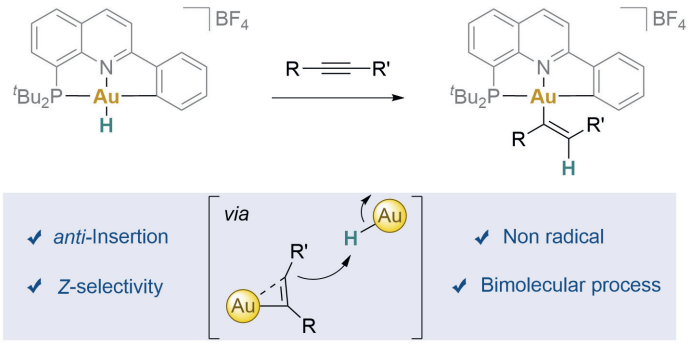
Alkyne hydrofunctionalization typically proceeds through *syn*-insertion into metal–hydride bonds; *anti*-insertion pathways are rare and not well understood. In this paper, the authors investigate the *anti*-insertion of alkynes into a gold(III)–hydride complex stabilized by a (P^N^C) ligand. They demonstrate that a range of terminal and internal alkynes, both activated and unactivated ones, undergo *anti*-Markovnikov addition to yield *Z*-vinyl gold species. A combination of mechanistic investigations — including radical trapping, deuterium-labeling, kinetic analysis, and DFT calculations — rules out previously assumed reaction pathways and indicates a non-radical, bimolecular insertion mechanism. Additionally, water significantly accelerates the reaction rate, likely by stabilizing a T-shaped gold(I) intermediate. This represents the first clear experimental evidence for *anti*-insertion into a gold(III)–hydride complex and opens new possibilities for using gold catalysis to build structural complexity.

Authors' comments:
"We report the regio- and stereoselective insertion of alkynes into a (P^N^C)gold(III) hydride *via* a bimolecular, nonradical mechanism wherein the Au-H formally behaves as a 'proton' source."



Peptide-Carbazolyl Cyanobenzene Conjugates: Enabling Biomolecule Functionalization *via* Photoredox and Energy Transfer Catalysis

Xing-Yu Liu, Wei Cai, Anne-Sophie Chauvin, Beat Fierz, and Jerome Waser*

Angew. Chem. Int. Ed. **2025**, e202507602
https://doi.org/10.1002/anie.202507602
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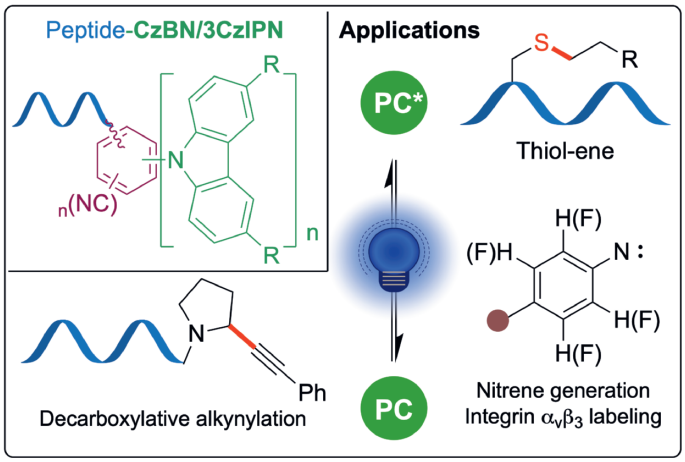
Waser and coworkers develop two methods to install carbazolyl cyanobenzene units on peptides for photocatalytic biomolecule functionalization. The first approach uses light-driven decarboxylation at the peptide's C-terminus to generate carbazolyl benzonitrile (CzBN) derivatives. The second exploits cysteine for selective SNAr with a fluorinated arene to form triscarbazolylisophthalonitrile (3CzIPN) conjugates. These conjugates maintain delayed fluorescence, improved redox potentials, and higher excited-state energies than standard cyanoarenes. Their photocatalytic activity enables peptide C-terminal decarboxylative alkynylation and cysteine selective thiol-ene reactions. Additionally, peptide-CzIPN conjugates facilitate protein labeling *via* aryl azide activation both *in vitro* and in cells. Incorporation of an integrin αvβ3-binding ligand further enables proximity-driven labelling. Overall, the study showcases cyanoarene–peptide conjugates as promising tools for biomolecule modifications in complex biological environments.

Authors' comments:
"These peptide–carbazolyl cyanobenzene conjugates hold great promise not only as alternatives to established Ir-based photocatalysts, but also for broader applications in biological contexts."



Prepared by Cesare Berton, James Southwell, Titouan Chetot, Jonas Genz, Stanislav Prytuliak, Fan Liu, Eda Nisli, Deborah Bäcker, Samy Kichou, Dominik Ernst, Tiago Rosa de Araujo, Liam Wenger, Ian Saxer, Laura Schüpke, Henrik Braband, and Jason P. Holland*
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Large Aromatic Amide Helices *via* Living Polycondensation

Dinh P. T. Nguyen, Saquib Farooq, Nicoleta Meyer, and Andreas F. M. Kilbinger*

Polym Chem **2025**, *16*, 2639.
https://doi.org/10.1039/D5PY00275C
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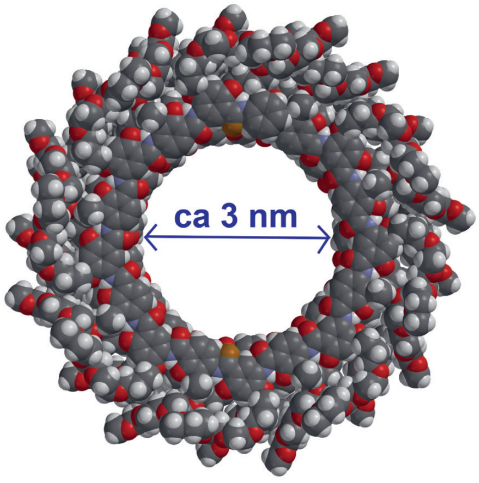
A living polycondensation method enables the synthesis of large aromatic amide helices with cavity diameters exceeding 1 nm, using an unsymmetrical backbone composed of AB-type amino acid monomers. These foldamers are stabilized by continuous three-center hydrogen bonds, allowing the formation of rigid helical structures. The polymerization, initiated by aniline and driven by chloro tri-o-tolyl phosphonium iodide (PHOS3), yields well-defined helices of controlled lengths. At higher target lengths, macrocyclic side products appear, attributed to self-initiation once the growing helix reaches a full turn. A 7-mer macrocycle was isolated and identified as the minimal unit needed to complete a full helical turn, providing key structural insights. When the initiator was omitted, self-condensation led predominantly to macrocycle formation, including 6-, 7-, 8-, and 9-membered species, with the 7-mer most abundant. This behaviour suggests a strong link between helical folding and macrocyclization kinetics. The method offers a streamlined, scalable route to unsymmetrical aromatic foldamers and macrocycles, expanding the toolkit for applications in host–guest chemistry, catalysis, and molecular transport.

Authors' comments:
"Being able to synthesize such large tubular structures is an important milestone for our group. Next, we will address longer tubes and those carrying functional groups on the inside of the helical cavity."



Small Organic Carbonic Anhydrase IX Ligands from DNA-Encoded Chemical Libraries for Tumor-Targeted Delivery of Radionuclides

Marco Müller, Tony Georgiev, Jacqueline Mock, Dario Neri, Samuele Cazzamalli*, and Sebastian Oehler*

J. Am. Chem. Soc. **2025**, *147*, 18230
https://doi.org/10.1021/jacs.5c05198
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This paper investigates the discovery and characterization of carbonic anhydrase IX (CAIX) ligands from DNA-encoded chemical libraries (DELs) for radionuclide imaging applications. CAIX is a promising tumor marker, especially in clear cell renal cell carcinoma (ccRCC) and hypoxic tumors. Its limited expression in most normal tissues makes it an excellent candidate for selective tumor imaging with radionuclides. As a method, DELs were screened against CAIX and the related isozyme CAII to identify highly selective ligands. Certain compounds were investigated *in vitro* (fluorescence polarization, SPR, flow cytometry) and *in vivo* (biodistribution in SK-RC-52 tumor-bearing mice). The lead candidate, named OncoCAIX, showed high affinity and selectivity for tumor tissue with up to 55% ID/g and very low uptake in healthy organs (tumor-to-kidney ratio >23). PET/CT imaging with [^{68}Ga]Ga-OncoCAIX confirmed rapid and selective tumor accumulation. OncoCAIX is a promising ligand for the non-invasive imaging of CAIX-positive tumors. A first-in-human clinical trial investigating [^{68}Ga]Ga-OncoCAIX is currently ongoing (NCT06840548).

Authors' comments:
"We used DELs to identify CAIX ligands with high affinity and selectivity for the target. The best performing candidate, named OncoCAIX, is now studied in the clinic with the prospect of helping kidney cancer patients in need."