



# Swiss Science Concentrates

A CHIMIA Column

Short Abstracts of Interesting Recent Publications of Swiss Origin

## A C–H activation-based enantioselective synthesis of lower carbo[n]helicenes

Shu-Min Guo, Soohee Huh, Max Coehlo, Li Shen, Grégory Pieters, and Olivier Baudoin\*

*Nat. Chem.* **2023**, *15*, 872–880

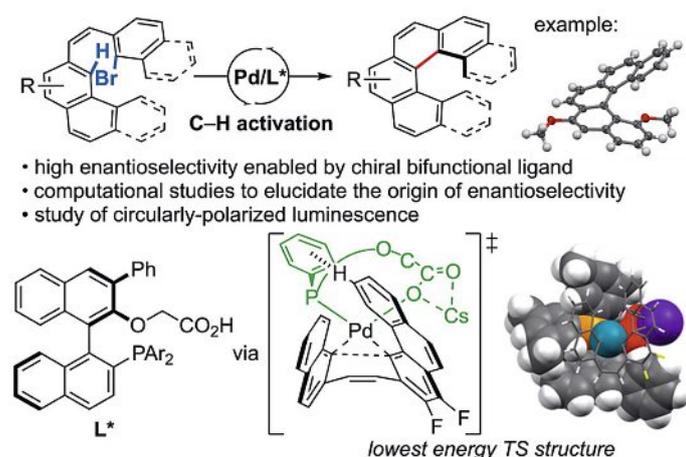
<https://doi.org/10.1038/s41557-023-01174-5>

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Carbohelicenes have a unique three-dimensional structure that has been exploited in various applications. Their strong circularly polarized luminescence has attracted attention for optical materials. However, there is still no direct catalytic enantioselective method for synthesizing lower, non-fused carbo[n]helicenes ( $n = 4–6$ ). In this study, a Pd-catalysed enantioselective C–H arylation using a bifunctional phosphine-carboxylate ligand was developed to access these compounds selectively. Computational studies suggested that the enantioselectivity arises from a combination of non-covalent interactions and steric repulsion during the C–H activation and reductive elimination steps. The photophysical and chiroptical properties of the synthesized scalemic [n]helicenes were studied. Overall, this method provides a simple and general access to lower carbo[n]helicenes with potential applications in optical materials.

### Authors' comments:

“Helicenes are important and fascinating, but also challenging to synthesize enantioselectively. C–H Arylation using chiral bifunctional ligands provides a conceptually simple solution to this synthetic problem.”



## To Fold or Not to Fold: Diastereomeric Optimization of an $\alpha$ -Helical Antimicrobial Peptide

Hippolyte Personne, Thierry Paschoud, Sofia Fulgencio, Stéphane Baeriswyl, Thilo Köhler, Christian van Delden, Achim Stocker, Sacha Javor, and Jean-Louis Reymond\*

*J. Med. Chem.* **2023**, *66*, 7570–7583

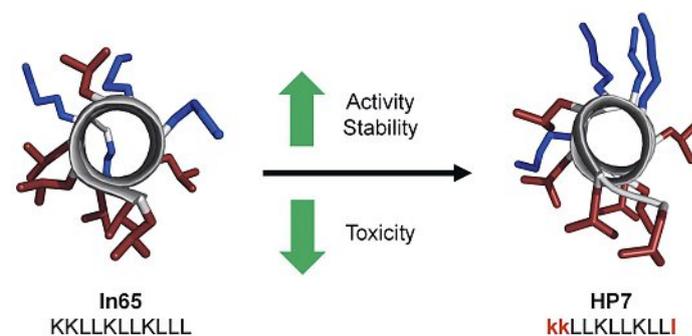
<https://doi.org/10.1021/acs.jmedchem.3c00460>

University of Bern

Membrane disruptive  $\alpha$ -helical antimicrobial peptides (AMPs) hold promise against multidrug resistance, but their toxicity and instability in serum pose challenges. Introducing D-residues can partially address these issues and reduce said toxicity without compromising antibacterial activity. The authors studied 31 diastereomers of the  $\alpha$ -helical AMP KKLLKLLKLLL to explore this potential and found three diastereomers with two, three, and four D-residues that exhibited increased antibacterial effects, comparable hemolysis, reduced toxicity to HEK293 cells, and excellent serum stability. X-ray crystallography confirmed that  $\alpha$ -helicity, as measured by circular dichroism, indicated  $\alpha$ -helical or disordered structures, regardless of chirality switched residues. Surprisingly, contrary to previous findings,  $\alpha$ -helicity across diastereomers correlated with antibacterial activity and hemolysis, revealing a complex relationship between stereochemistry, activity, and toxicity. These results highlight the potential of diastereomers for optimizing properties of AMPs, offering new avenues for combating multidrug resistance.

### Authors' comments:

“Simple stereochemical changes in peptides sequence can have beneficial impact on their properties. In the context of multidrug resistant pathogens, this opens a large unexplored easy-to-access chemical space for property optimization.”



## Electron-Driven Nitration of Unsaturated Hydrocarbons

Subrata Patra, Ivan Mosiagin, Rahul Giri, Thomas Nauser, and Dmitry Katayev\*

*Angew. Chem. Int. Ed.* **2023**, e202300533

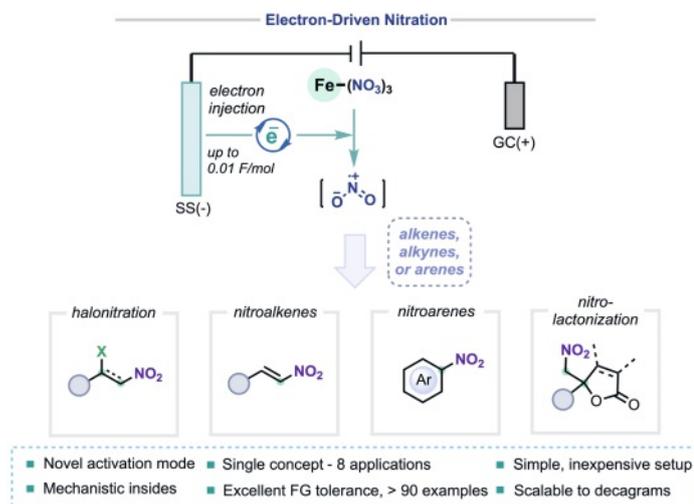
<https://doi.org/10.1002/anie.202300533>

University of Bern and University of Fribourg

Traditional methods for the synthesis of nitroalkenes involve harsh conditions and toxic reagents, necessitating the development of more sustainable and selective alternatives. The electron-driven nitration of unsaturated hydrocarbons represents a promising approach to achieving this goal. This paper addressed this challenge by using electrons as the catalyst and demonstrated that unsaturated hydrocarbons including alkenes, alkynes, and arenes can be nitrated under electron-catalyzed conditions with high levels of chemo- and regioselectivity, and with exceptional functional group tolerance. The mechanism involves the formation of a transient radical intermediate, which undergoes a series of electron transfer steps to give the final product. This study provides insights into the factors that govern the selectivity of the reaction and offers a more sustainable approach to the synthesis of nitrogen-containing compounds.

### Authors' comments:

“Direct nitration methods mostly rely on the formation of nitronium ( $\text{NO}_2^+$ ) ion in highly caustic nitric acid mixtures, which results various limitations on practical use. Herein, we introduce an electron-catalyzed protocol for the generation of nitryl radical from ferric nitrate under mild and non-acidic reaction conditions.”



## Directional Ionic Bonds

Illia Hutskalov, Anthony Linden, and Ilija Čorić\*

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<https://doi.org/10.1021/jacs.3c01030>

University of Zurich

Covalent bonds are characterized by strong directionality, whereas ionic bonds lack such characteristics due to the absence of directionality of electric field around simple ions. Unlike usual ionic bonds, which are formed between oppositely charged ions in a random orientation, directional ionic bonds occur when ions are aligned in a specific orientation that maximizes electrostatic attraction. Herein, the authors report the achievement of predictable directionality of ionic bonding by using concave nonpolar shields around the charged sites. Various ionic compounds were analyzed and their structures can be explained by the directional bonding model. The results suggest the potential use of directional ionic bonding in the design and development of new materials with tailored properties.

### Authors' comments:

“Directional ionic bonds represent a distinct directional noncovalent interaction for three-dimensional structuring at the molecular level. Similar to hydrogen bonds, they could find broad use in supramolecular and materials chemistry.”

