Machine learning assisted design of heteromeric self-assembled molecular capsules

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Catalysis in hydrogen bond-based supramolecular capsules is the main research direction in the Tiefenbacher group. Much like enzymes, such capsules feature a nanometer-sized cavity where suitable reactions can be accelerated due to noncovalent interactions between the substrate and host. Interesting results concerning complex terpene cyclizations, which were inaccessible with man-made catalysts before, have been obtained in our laboratory (for more information see: https://nanocat.chemie.unibas.ch/en/research/). Although these examples clearly demonstrated the potential of this approach, selectivity issues remain. Due to the high symmetry of the nanometer-sized reaction compartment on the inside of the molecular capsule, the conformation of the flexible acyclic terpene substrates cannot be controlled well. The floppy binding translates into a poor selectivity during terpene cyclizations. To achieve selective cyclizations for biologically relevant sesqui- and diterpenes, less symmetric cavities, able to constrain the conformationally freedom of the encapsulated the substrate, are required.

The overall aim of this project is the discovery of novel heteromeric self-assembled molecular capsules suitable for selective sesqui- and diterpene cyclizations. Since there is no rational approach available, we aim for a broad screening approach aided by machine learning algorithms developed in the von Lilienfeld lab (for more information see: https://chemspacelab.org/). To be able to successfully work on this project, skills in organic synthesis as well as programming are required.