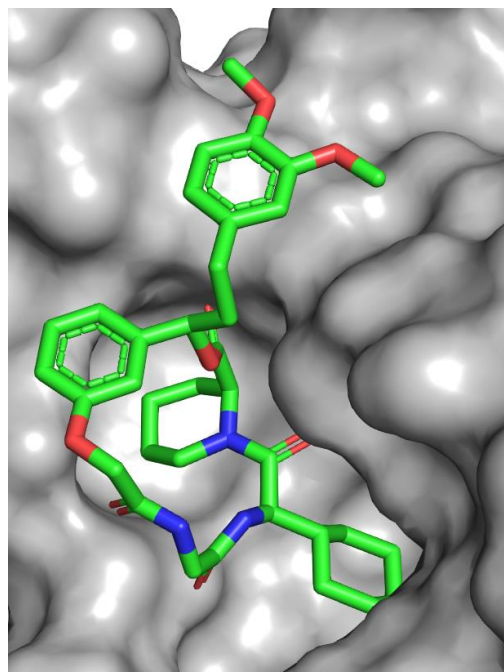
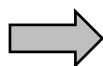
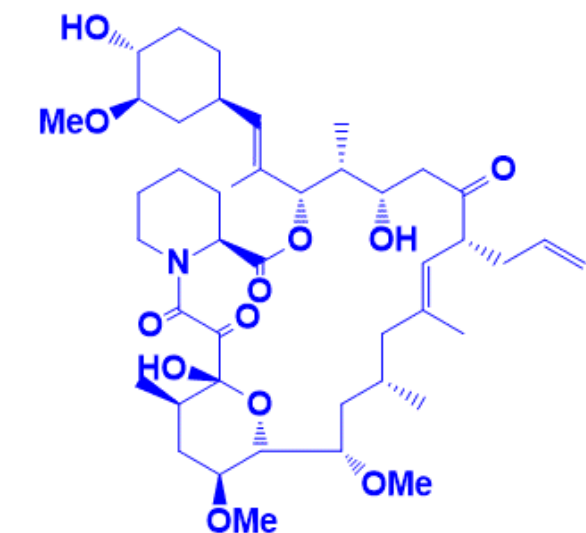


# Two PhD positions in macrocyclic drug discovery

Develop synthetic approaches for the assembly of complex natural product-like macrocycles & application to the identification of inhibitors for the FK506-binding protein 51 (FKBP51), a key drug target for depression, obesity & chronic pain.



**Topic 1:** Conformation control by post-cyclization derivatization & rigidification

**Aim:** A fine-tuned balance between flexibility and rigidity underlies many of the beneficial properties of MCs. To better control this, conformational pre-organization will be achieved by the incorporation of rigid building blocks and by the development and application of tailored derivatization reactions that introduce rigidity and functional diversity on pre-assembled macrocycles.

**Topic 2:** Permeability & polarity control by combinatorial macrocycle assembly

**Aim:** Properly configured macrocycles allow a unique combination of high cell permeability and high polarity, which makes them particularly attractive for difficult drug targets. To exploit this more systematically, polar groups will be introduced in a systematic manner to foster intramolecular contacts and to the target proteins. This approach will be extended to macrocyclic molecular glues.

**Where:** Technical University Darmstadt, Institute of Organic Chemistry & Biochemistry

**Suited for:** Organic chemists interested in biology, pharmacology & drug discovery

**Requirements:** Master degree in chemistry, with a specialization in organic chemistry

**We offer:** Training in modern medicinal chemistry and dedicated mentoring in an interdisciplinary and international lively group, embedded in the [MSCA consortium MC4DD](#).

**Literature:** Voll et al., *Angew Chem Int Ed* 2021, [doi:10.1002/anie.202017352](https://doi.org/10.1002/anie.202017352)  
Bauder et al., *J Med Chem* 2021, [doi:10.1021/acs.jmedchem.0c02195](https://doi.org/10.1021/acs.jmedchem.0c02195)  
Krajczyk et al., *Chem Eur J* 2024, [doi:10.1002/chem.202401405](https://doi.org/10.1002/chem.202401405)

**Main mentor & further infos:** Prof. Felix Hausch, [felix.hausch@tu-darmstadt.de](mailto:felix.hausch@tu-darmstadt.de),  
[https://www.chemie.tu-darmstadt.de/hausch/rg\\_hausch/index.en.jsp](https://www.chemie.tu-darmstadt.de/hausch/rg_hausch/index.en.jsp)