FAKULTÄT FÜR CHEMIE

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Einladung zum Vortrag von

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„Synthesis-enabled probes for Chemical Biology"

Chemical probes to study biological systems by acute and reversible perturbation in space and time enable the discovery and utilization of biomolecular interactions and pathways by means which are orthogonal to physical or genetic methods. Historically often lacking systematic evidence and hence referred to as the "pharmacological approach" in biology, chemical probes today constitute the core of a growing area of discovery driven research in chemical biology. Furthermore, they allow superb interconnection with drug design and potential translation to therapeutic approaches.
In our view, chemical probes offer excellent opportunities for organic synthesis as well: They transform the areas of target-oriented natural product synthesis and traditional medicinal chemistry into a wider chemical space. Therefore, in our research we aim at utilizing the power of chemical synthesis to create unique chemical probes unavailable to nature and its biosynthesis machinery, and, on the other hand, investigate yet unexplored or unused molecular mechanism by tracking bioactive probes' functioning in biology.
Three case studies will be presented in the seminar. Firstly, the chemical synthesis of thiopeptide antibiotics as probes will be discussed.[1] However, beyond the antibiotic activity and potential applications e.g. for tuberculosis therapy, which will be covered, thiopeptide antibiotics trigger gene transcription by a ligand-activated bacterial transcription factor system that is widespread in bacteria. Secondly, the transformation of actin-binding natural products into chemical probes will be demonstrated.[2] From chemical synthesis and SAR studies, non-toxic probes that allow staining of actin in living cells were derived. By judicious chemical modification, these probes could recently be converted into tool compounds that can control the dynamics of the actin cytoskeleton in response to light stimuli. Thirdly, dihydropyridines that specifically block protein transport will be introduced.[3] The discovery of the dihydropyridine probes, their validation and their optimization will be discussed. Furthermore, during the course of this study the mechanism of the crossed Hantzsch dihydropyridine synthesis was reinvestigated, leading to a novel, consistent model for the reaction mechanism.

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