

PLENARY PRESENTATIONS

CHEMO-ENZYMATIC SYNTHESIS OF NUCLEOSIDE ANALOGS: THERMODYNAMIC REACTION CONTROL VS KINETICS

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Nucleoside analogs are an important class of antiviral and anticancer acting drugs [1, 2]. Of special pharmacological interest are analogs carrying halogenated nucleobase derivatives or modified sugar moieties, but also derivatives of the successful antiviral agent ribavirin, a 1,2,4-triazole-containing purine analog [3]. Enzymes involved in nucleoside metabolism have been shown to be a valuable addition to the methodological toolbox for nucleoside analog synthesis [4]. The chemo-enzymatic processes typically involve Nucleoside Phosphorylases, which catalyze the thermodynamically controlled reversible phosphorolysis of nucleosides [5]. Different optimization strategies for these kinds of reaction systems have been developed by our group and others over the years, some of which will be discussed in the talk. As example case serves a screening of mesophilic and thermophilic bacterial and archaeal Nucleoside Phosphorylases from our library for their ability to use 3-thio-1,2,4-triazole-containing nucleobase analogs. Interestingly, the tested NPs showed distinct substrate preferences, despite of the high level of active site conservation between them. Furthermore, we could show that the reactions are thermodynamically controlled and can thereby be optimized for yield.

Referens:

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