Enzyme-Independent Chemical Reactions for Chemistry in Living Cells

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Enzyme-independent chemical reactions, which are orthogonal to intracellular processes, may be used for design of novel disease-specific prodrugs and for monitoring biomolecules (e.g. proteins, nucleic acids) and biochemical states (e.g. inflammation). Therefore, they can be applied for both the treatment of diseases and their diagnostics. [1]

Bond-forming reactions compatible with live cells, which can be templated by nucleic acids, are investigated in this project.

The purpose of these theoretical investigations is to provide support to synthetic groups in the selection of appropriate substrates.

In order to find the proper systems to react, we initially investigated the reaction pathways of different simple nucleophiles and electrophiles such as aliphatic and aromatic organo-selenolates, thiolates, thiols, with different types of organochlorides. The same investigations were performed for bigger nucleophiles as glutathione (GSH and GS-) and thioredoxin reductase (TrxR).

Our results show that reactions of the aliphatic organoselenolate and TrxR with organochloride have the lowest reaction energy barrier compared to the other systems calculated. We will now extend our reaction systems towards more complex systems and compare these to the available experimental data.

[1] M. Yang at al, *Chem. Soc. Rev.*, **2014**, *43*, 6511.