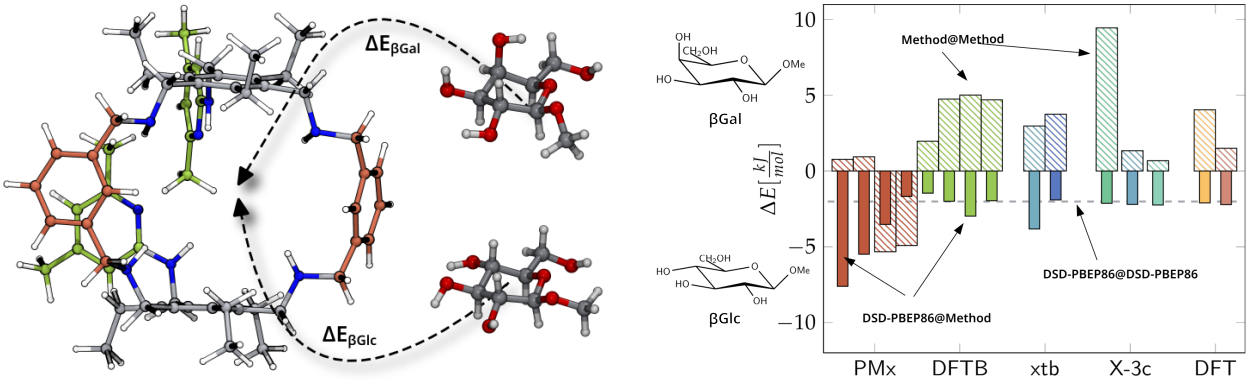
Selective complexation of carbohydrates with artificial receptors - A computational challenge

Conrad Hübler and Monika Mazik
Institut für Organische Chemie, Technische Universität Freiberg, Leipziger Straße 29, 09599 Freiberg

Carbohydrates play a key role in a wide range of biological processes and the detailed understanding of the principles of their recognition by carbohydrate-binding proteins is of particular interest for researchers. Biomimetic carbohydrate receptors [1-3] provide valuable model systems to study the underlying principles of carbohydrate-based molecular recognition events and their development is also strong motivated by the belief that such artificial carbohydrate-binding agents could be used for the detection and treatment of diseases. Although effective artificial receptors have been developed, the exact prediction of their binding strength and selectivity is still further away and it is hoped that combined theoretical and experimental studies will contribute significantly to the solution of this problem.

Our previous studies showed that receptors consisting of both a macrocyclic building block and flexible side-arms [4-6] exhibit strong selectivity towards *β*-D-glucoside and represent particularly interesting objects for systematic binding studies. The binding capabilities of these receptor molecules were determined by investigations in two-phase systems, such as liquid-liquid extractions of sugars from water into organic phase, and by studies in homogenous media, including ^{1}H NMR, fluorescence and microcalorimetric titrations.



We present the calculational study of the selectivity of macrocyclic carbohydrate receptors towards methyl *β*-D-glycosides, such as gluco- and galactopyranoside, using popular semiempirical quantum-chemical and quantum-chemical methods, combined with an analysis of the potential energy surface (PES). The PES of the glycosides was sampled using molecular dynamics and simulated annealing while the PES of the complexes of the macrocyclic receptors with the bound substrates was sampled using a simplified docking procedure. The selectivity towards the carbohydrates is then calculated at different levels of theory. Although the calculated selectivity indicates better binding of *β*-methylglucoside for most of these samples, the results elucidate the difficulties of modelling flexible molecules (including carbohydrates) and more studies have to be carried out.

[1] Mazik, M. *RSC Adv.* **2012**, *2*, 2630. [2] Davis, A. P. *Org. Biomol. Chem*. **2009**, *7*, 3629. [3] Mazik, M. *Chem. Soc. Rev.* **2009**, *38*, 935. [4] Lippe, J.; Mazik, M. *J. Org. Chem.* **2015**, *80*, 1427. [5] Lippe, J.; Mazik, M. *J. Org. Chem.* **2013**, *78*, 9013. [6] Amrhein, F.; Lippe, J.; Mazik, M. *Org. Biomol. Chem*. **2016**, *14*, 10648.