

Tsuji-Trost allylation for chemoselective modification of cysteines within peptides and proteins

Speaker: Julia Kriegesmann
Email: julia.kriegesmann@univie.ac.at
Institute: Institute of Biological Chemistry

Prenylation is a posttranslational modification which is important for the association of certain proteins to specific membranes.[1] Our current knowledge about the physiological function of many of these proteins is mostly based on the use of prenylated peptides that are linked to a target protein by chemoselective reactions such as native chemical ligation in order to produce prenylated protein variants.[1-3] Other approaches to prepare protein variants with either natural or synthetically modified residues are based on enzymes or selective chemical modification of proteins. The latter allows to decide which modification should be attached to which residue in order to create proteins with the desired properties such as natural posttranslational modifications, fluorophores or reactive tags. However, the synthesis of prenylated peptides and proteins still represents a severe challenge due to problems with chemoselectivity, reaction conditions and yield.[4] Therefore new methods to selectively introduce modifications leading to native posttranslational modifications as introduced by prenyltransferases in nature are needed.

Here we demonstrate that the Pd-catalyzed Tsuji-Trost-allylation can be used for the prenylation of Cys-containing peptides and proteins. By this, prenylated peptides and proteins can be accessed, with high n/iso ratio and excellent chemoselectivity. Furthermore, it is possible to introduce other modifications such as a fluorophore, an affinity tag or staples into peptides by this reaction.

- [1] L. Brunsveld, J. Kuhlmann, K. Alexandrov, A. Wittinghofer, R. S. Goody, H. Waldmann, *Angew. Chem. Int. Ed.* **45** (2006), 6622–6646.
- [2] T. Mejuch, H. Waldmann, *Bioconjugate Chem.* **27** (2016), 1771–1783.
- [3] B. Ludolph, H. Waldmann, *Chem. Eur. J.* **9** (2003), 3683–3691.
- [4] O. Boutureira, G. J. L. Bernardes, *Chem. Rev.* **115** (2015), 2174–2195.