

Synthesis of C-glycosylated amino acids

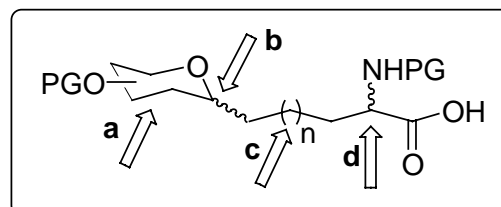
Glycopeptides are of growing interest because they are involved in many biological processes like cell recognition and cell-cell communication. In contrast to the natural *O*- and *N*-glycopeptides, *C*-glycopeptides are more stable against chemical and enzymatic hydrolysis.

The topic of our investigations is the development of simple and easy ways to synthesize *C*-glycopeptides. Two new methods for the synthesis to *C*-glycosylated amino acids have been developed. These two synthetic approaches are quite different but both begin with the same carbohydrate building block. The carbohydrate building block is *C*-alkylated with an alkenyl side chain at the C-1 position.

The first approach utilizes the unsaturated side chain for a stereoselective [2+3]-cycloaddition with an chiral non-racemic nitron. The nitron is synthesised from glycine and (+)- or (-)-menthone as chiral auxiliary. After cleaving the auxiliary from the cycloaddition product the free *C*-glycosylated amino acid is obtained.

The second approach uses the unsaturated side chain for an intramolecular Grubbs olefin metatheses with an unsaturated amino acid. After opening the lacton orthogonally protected *C*-glycosylated amino acid can be obtained.

Both synthesis to *C*-glycosylated amino acids are very simple and afford the products in only three steps in high yields. The structural diversity of the *C*-glycosylated amino acids is very high. The varied parameters are:



- a great variety of carbohydrates can be used (glucose, galactose, mannose, GlcNAc, GalNAc, pseudo-glycal and others are possible) (arrow a),
- a α - and β -selective synthesis is possible (arrow b),
- different amino acids can be used, especially quarternary amino acids (arrow c),
- a selective synthesis to D- and L- amino acid is possible (arrow d),
- all comenly used protecting groups can be employed,
- connecting to a solid phase is possible,
- glycosylation during a peptide synthesis is possible.