

## Stereocontrolled Synthesis of Monosaccharides from Dihydroxyacetone

Oskar Popik

Supervisor: prof. Jacek Młynarski

In nature carbohydrates are synthesized by enzyme-catalyzed aldol reactions. Four naturally occurring D-ketohexoses are formed in a stereoselective aldol addition of D-glyceraldehyde-3-phosphate to dihydroxyacetone phosphate promoted by four different aldolase enzymes. The development of organocatalysis allowed to mimic enzymes' mode of action while expanding the substrate scope.

Herein, I present an organocatalytic method for the *de novo* synthesis of *syn*-configured ketohexoses. Formation of fructose and sorbose of both D and L series was possible in a direct aldol reaction of unprotected dihydroxyacetone (DHA) with both (*R*)- and (*S*)-glyceraldehyde acetonides in the presence of water. The developed  $C_2$ -symmetrical serine-based organocatalysts mimic nature's aldolase enzymes and allow for the formation of all *syn*-configured ketohexoses in good yields and high selectivities. The enamine mechanism of the reaction was proven by enantioselective direct *syn*-aldol reaction of unprotected dihydroxyacetone with achiral aldehydes. An additional proof came from the HRMS (ESI) spectrum of the enamine formed *in situ* from siloxyserine organocatalyst and dihydroxyacetone.

I have also demonstrated the possibility of application of primary, secondary and tertiary amines as catalysts for the aldol reaction of unprotected dihydroxyacetone with (*R*)-glyceraldehyde acetonide. These reactions result in a stereoselective formation of D-fructose as a result of a general base mechanism by the Felkin-Anh model.

The developed serine-based organocatalysts were also used for the highly stereoselective synthesis of naturally occurring higher carbon sugars. This methodology gave access to sedoheptulose and D-*glycero*-L-*galacto*-oct-2-ulose in a direct aldol reaction of unprotected dihydroxyacetone with D-erythrose and D-xylose, respectively.

Finally, bis(siloxyserinamide) organocatalyst gave access to L-fructose. This unnatural sugar was synthesized as a single diastereoisomer in a gram scale. The  $C_2$ -symmetrical bis(amide) catalysts were also used in an direct aldol reactions leading to C-glycosides with high yields and selectivities.