

THE SUMMARY OF Ph. D. DISSERTATION

Major Applied Chemistry		SURNAME, Firstname TOTANI, Kiichiro
<p>Title</p> <p>Development of Stereoselective Synthetic Organic Reactions Using Carbohydrate-derived Asymmetric Environments</p>		
<p>Abstract</p> <p>In the fields of asymmetric synthesis, one of the most important subjects in modern synthetic organic chemistry, methods using asymmetric environments derived from natural products have been widely utilized. And various stereoselective synthetic organic reactions using amino acids, alkaloids or terpenoids as steric environments have been reported. Carbohydrate-derived asymmetric environments, as compared with those derived from other natural products, have not been widely investigated.</p> <p>However, carbohydrates have two convenient features to construct various asymmetric environments. One is an abundant amount, and the other is a variety of stereoisomers. In this dissertation, the author describes five diastereoselective carbon-carbon bond-forming reactions achieved on various carbohydrate templates.</p> <p>1. Stereoselective 1,4-additions of organocopper reagents</p> <p>The variety of substrates, containing asymmetric environment around α,β-unsaturated ester part as a reaction site, were prepared from methyl α-D-glucoside, α-D-mannoside or α-D-galactopyranoside. The 1,4-additions of various organocopper reagents, derived from corresponding Grignard reagents, to the substrates were proceeded with high diastereoselectivities. <i>re</i>-Face adducts and <i>si</i>-face adducts were also obtained selectively by using different types of carbohydrate templates properly. Moreover, the methods for removal of the carbohydrate template from 1,4-adducts and recycling the template were established. These methods could be applied to the all products described below.</p>		

2. Stereoselective 1,4-additions of organolithium reagents

1,4-Additions of various organolithium reagents to the substrates, which provided *re*-face adducts stereoselectively in 1,4-additions of organocopper reagents, were proceeded with high diastereoselectivities to provide *si*-face adducts. According to these results, a desired stereoisomer could be obtained from same substrate by selection of the nucleophile, i.e. organocopper reagent or organolithium reagent.

3. Stereoselective α -alkylation

α -Alkylations to propionyl ester or phenylpropionyl ester containing glucopyranosidic template were performed with high yields and high stereoselectivities using NaHMDS as a base. These results showed that asymmetric induction at α - and β -positions of esters could be achieved by using the concept of which the author proposed.

4. Stereoselective 1,4-addition/ α -alkylations

In this section, the author applied the concept of carbohydrate-induced stereoselective reactions for constructions of vicinal asymmetric centers.

The substrate was same as the one for 1,4-additions. α -Methylation to the 1,4-phenyl adducts obtained in section 1 or 2 provided (2*S*,3*R*)-*syn*- or (2*S*,3*S*)-*anti*-isomer in highly stereoselective manner, respectively (stepwise method). On the other hand, α -methylations were also proceeded *in situ* in the case of methyl iodide was added after 1,4-additions of phenylcopper reagent or phenyllithium reagent (one-pot method) to provide the same (2*S*,3*R*)-*syn*- or (2*S*,3*S*)-*anti*-isomer both with high stereoselectivities, respectively.

5. Stereoselective 1,4-addition/ α -protonations

1,4-Addition of phenyllithium to the tigloyl ester, containing glucopyranosidic template same as the one using in section 4, and followed by α -protonation by *i*-PrOH proceeded with high stereoselectivity to provide the (2*R*,3*S*)-*syn*-isomer, different from the *syn*-isomer obtained in section 4.