

## 【Grant-in-Aid for Scientific Research (S)】

Biological Sciences (Medicine, Dentistry, and Pharmacy)



### Title of Project : Regioselective Molecular Transformation of Multifunctionalized Molecules

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Research Area : Synthetic Organic Chemistry

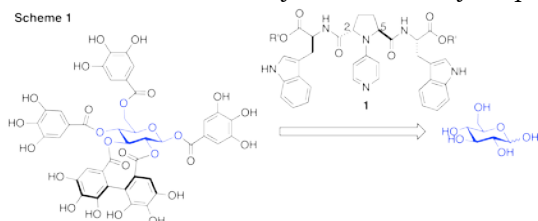
Keyword : carbohydrate, peptide, supramolecule, molecular recognition, asymmetric synthesis

#### 【Purpose and Background of the Research】

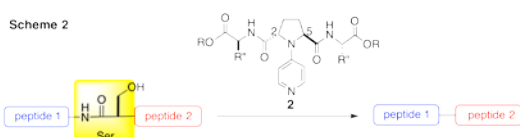
Regioselective manipulation of multifunctionalized molecules such as carbohydrates has been developed via a multi-step protection-deprotection strategy based on the intrinsic reactivity of the substrate molecules. Direct regioselective transformation without protection-deprotection processes has been a long-standing object in organic synthesis. We aim to develop the methods for catalyst-controlled regioselective molecular transformation of multifunctionalized molecules, which includes those for short-step total syntheses of natural glycosides from unprotected D-glucose and regioselective cleavage of peptides under neutral conditions. Catalytic discrimination of supramolecular topological chirality will be also investigated.

#### 【Research Methods】

Catalyst **1** effectively promotes regioselective acylation at intrinsically less reactive C(4)-OH among four free hydroxy groups of glycopyranoses. We plan to develop a short-step total syntheses of natural glycosides starting from unprotected glucose via regioselective molecular transformation with catalyst **1** at the key step.

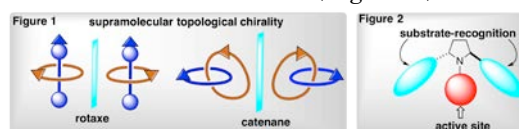


Catalyst **2** promotes regioselective peptide cleavage under neutral conditions at an ambient temperature. Scope and limitation of this reaction is examined.



Dissymmetric achiral components constitute topological chirality in the formation of supramolecules such as rotaxanes and catenanes. Catalytic discrimination of this type of mobile topological chirality is investigated (Figure 1).

Regioselective molecular transformations in Schemes 1 and 2 can be achieved under fine molecular recognition by catalyst **1** and **2**. The amide side chains at C(2) and C(5) of the pyrrolidine skeleton are expected to be responsible for the molecular recognition. We plan to create new catalysts consisting of the side chains for molecular recognition and an active site toward the development of regioselective molecular transformations (Figure 2).



#### 【Expected Research Achievements and Scientific Significance】

Unconventional approaches toward the synthesis and molecular transformation of ubiquitous molecules of biological interest such as carbohydrates and peptides will be developed. These approaches include (1) catalyst-controlled total synthesis of natural glycosides starting from D-glucose without using protective groups for glucose, and (2) regioselective peptide cleavage of serine-containing peptides. Approaches toward catalytic discrimination of topological chirality of supramolecules such as rotaxanes and catenanes will also be shown. A new catalyst design toward regioselective molecular transformations is also proposed. This project will contribute to open a new phase in organic synthesis.

#### 【Publications Relevant to the Project】

- Kawabata, T.; Muramatsu, W.; Nishio, T.; Shibata, T.; Schedel, H. "A Catalytic One-Step Process for the Chemo- and Regioselective Acylation of Carbohydrates", *J. Am. Chem. Soc.* **129**, 12890-12895 (2007).
- Yoshida, K.; Mishiro, Ueda, Y.; Shigeta, Furuta, T.; Kawabata, T. "Nonenzymatic Geometry-Selective Acylation of Tri- and Tetrasubstituted  $\alpha,\alpha'$ -Alkenediols", *Adv. Synth. Catal.* **354**, 3291-3298 (2012).

【Term of Project】 FY2014-2018

【Budget Allocation】 93, 600 Thousand Yen

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