

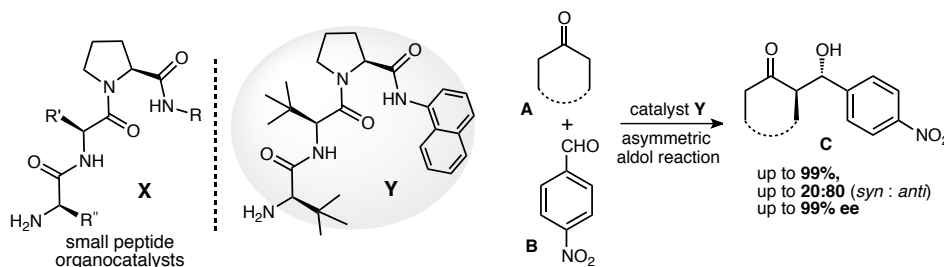
New Type Novel Small Peptide Organocatalyst for Asymmetric Aldol Reaction of Various Ketones with Aldehydes

(¹Division of Sustainable and Environmental Engineering, Graduate School of Engineering, Muroran Institute of Technology, ²Tohoku Medical and Pharmaceutical University, ³Research and Analytical Centre for Giant Molecules, Graduate School of Sciences, Tohoku University, ⁴Tokiwakai Group) ○ Rajkumar Thiyagarajan,¹ Zubeda Begum,¹ Chigusa Seki,¹ Yuko Okuyama,² Eunsang Kwon,³ Koji Uwai,¹ Michio Tokiwa,⁴ Suguru Tokiwa,⁴ Mitsuhiro Takeshita⁴ and Hiroto Nakano¹

Keywords: Organocatalyst; Amino Acid; Peptide; Asymmetric Reaction; Aldol Reaction.

The development of new chiral organocatalyst is very important for obtaining of a chiral product with a high optical purity in a catalytic asymmetric reaction. Therefore, the development of an effective organocatalyst for this reaction is a significantly challenging task. Most recently, we have developed chiral amino amide organocatalyst showing a high level of catalytic activities in some asymmetric reactions.¹ Recently, small synthetic peptides have been demonstrated to be effective catalysts for an increasingly wide array of asymmetric reactions.² In many cases, these peptide catalysts have enabled novel multifunctional substrate activation modes and unprecedented selectivity manifolds.

In this study, new small peptide organocatalyst **X** confused both proline amide and dipeptide sites in the single molecule was designed and synthesized as a new small peptide organocatalyst. This catalyst contains a primary amino group acting as an enamine formation site as well as hydrogen bond formation site, secondary amide groups for forming hydrogen bonding site to fix substrates for obtaining superior stereoselectivities in an asymmetric reaction. Furthermore, pyrrolidine ring of proline amide as backbone, alkyl or aryl groups on the peptide chain and also polycyclic aromatic groups on amide group may act as a steric and electronic influences sites. The catalytic capability of the obtained organocatalyst **X** was tried in the asymmetric aldol reaction of various ketones **A** with aldehydes **B**. The aldol reaction is one of the most versatile reaction for the constructions of carbon-carbon bond formation reaction.³ As a results, the peptide catalyst **Y** showed good to excellent catalytic activities in this reaction to afford the corresponding chiral aldol products **C** in good to excellent chemical yields (up to 99%) and stereoselectivities [up to *syn:anti* 20:80, up to 99% *ee* (*anti*)].



1) I.A. Owolabi, U.V. Subba Reddy, M. Chennapuram, C. Seki, Y. Okuyama, E. Kwon, K. Uwai, M. Tokiwa, M. Takeshita, H. Nakano, *Tetrahedron*, **2018**, 76, 4705. 2) W. Huang, H. Tian, H. Xu, L. Zheng, Q. Liu and S. Zhang, *Catal. Lett.*, **2011**, 141, 872. 3) K. Sakthivel, W. Notz, T. Bui, C.F. Barbas, *J. Am. Chem. Soc.*, **2001**, 123, 5260.