Division of Synthetic Chemistry
– Synthetic Organic Chemistry –

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Prof
KAWABATA, Takeo
(D Pharm Sc)

Assist Prof
UEDA, Yoshihiro
(D Pharm Sc)

Assist Prof
MORISAKI, Kazuhiro
(D Pharm Sc)

Techn Staff
FUJIHASHI, Akiko

Students

CHEN, Gong (D3)
XING, Yongning (D3)
NINOMIYA, Ryo (D3)
HASHIMOTO, Hisashi (D2)
EMI, Ryota (M2)
SHIGEMATSU, Hajime (M2)
FUJIMURA, Kouki (M2)
TANIGAKI, Yusuke (M1)
UJI, Akihito (UG)

Scope of Research

The research interests of this laboratory include the development of advanced molecular transformation, total synthesis of biologically active products, and molecular recognition. Programs are active in the following areas: 1) asymmetric alkylation of carbonyl compounds based on “memory of chirality”, 2) organocatalysis for fine organic syntheses, 3) synthesis of unusual amino acids and nitrogen heterocycles, 4) regioselective functionalization of carbohydrates, and 5) the structural and functional investigation of heterochiral oligomers.

KEYWORDS

Site-Selective Functionalization
Molecular Recognition
Organocatalysis
Dynamic Chirality
Unusual Amino Acid

Selected Publications

Kawabata, T.; Moriyama, K.; Kawakami, S.; Tsubaki, K., Powdered KOH in DMSO: An Efficient Base for Asymmetric Cyclization via Memory of Chirality at Ambient Temperature, *J. Am. Chem. Soc.*, **130,** 4153-4157 (2008).

Kawabata, T.; Jiang, C.; Hayashi, K.; Tsubaki, K.; Yoshimura, T.; Majumdar, S.; Sasamori, T.; Tokitoh, N., Axially Chiral Binaphthyl Surrogates with an Inner N-H-N Hydrogen Bond, *J. Am. Chem. Soc.*, **131,** 54-55 (2009).

Yoshida, K.; Furuta, T.; Kawabata, T., Organocatalytic Chemoselective Monoacylation of 1, *n*-Linear Diol, *Angew. Chem. Int. Ed.*, **50,** 4888-4892 (2011).

Hamada, S.; Furuta, T.; Wada, Y.; Kawabata, T., Chemoselective Oxidation by Electronically Tuned Nitroxyl Radical Catalysts, *Angew. Chem. Int. Ed.*, **52,** 8093-8097 (2013).

Tomohara, K.; Yoshimura, T.; Hyakutake, R.; Yang, P.; Kawabata, T., Asymmetric α-Arylation of Amino Acid Derivatives by Clayden Rearrangement of Ester Enolates via Momory of Chirality, *J. Am. Chem. Soc.*, **135,** 13294-13297 (2013).

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Takeuchi, H.; Mishiro, K.; Ueda, Y.; Fujimori, Y.; Furuta, T.; Kawabata, T., Total Synthesis of Ellagitannins via Regioselective Sequential Functionalization of Unprotected Glucose, *Angew. Chem. Int. Ed.*, **54,** 6177-6180 (2015).

Ueda, Y.; Furuta, T.; Kawabata, T., Final-Stage Site-Selective Acylation for the Total Syntheses of Multifidosides A-C, *Angew. Chem. Int. Ed.*, **54,** 11966-11970 (2015).

Imayoshi, A.; Lakshmi, B.; Ueda, Y.; Yoshimura, T.; Matayoshi, A.; Furuta, T.; Kawabata, T., Enantioselective Preparation of Mechanically Planar Chiral Rotaxanes by Kinetic Resolution Strategy, *Nat. Commun.*, **12,** 404 (2021).

Enantioselective Preparation of Mechanically Planar Chiral Rotaxanes by Kinetic Resolution Strategy

The field of asymmetric synthesis is becoming a mature science. On the other hand, asymmetric synthesis of chiral mechanically interlocked molecules such as mechanically planar chiral rotaxanes and topologically chiral catenanes (Figure 1) has been rather unexplored, and their highly enantioselective synthesis has been a long-standing dream in organic synthesis. Here we report our efforts toward this goal. The strategy relies on kinetic resolution of racemic mechanically planar chiral rotaxanes by catalytic asymmetric acylation of the hydroxy group (Figure 2a). An expected problem was determining how can such remote asymmetric induction be achieved? Methods for acylative kinetic resolution of racemic alcohols have been extensively investigated, and efficient discrimination of chirality of substrate alcohols has been achieved when the reacting center (OH) in the substrate is close to the chiral center (Figure 2b). On the other hand, discrimination of the chirality of the substrate by acylation of the hydroxy group located at the edge of the huge mechanical interlocked molecule may not be readily achievable (Figure 2a). However, use of our original catalyst accomplished the objective. Kinetic resolution of the racemic rotaxane **1** was performed with catalyst **2** via remote asymmetric acylation of a hydroxy group in the axis component to successfully provide an unreacted enantiomer in up to >99.9% ee in 29% yield (Figure 3) (The theoretical maximum yield of kinetic resolution of racemate is 50%). While the rotaxane molecule is expected to have conformational complexity, catalyst **2** enabled to discriminate the mechanical chirality of the rotaxanes efficiently with the selectivity factors in up to 16 (*Nat. Commun*. **2021**, 12, 404).

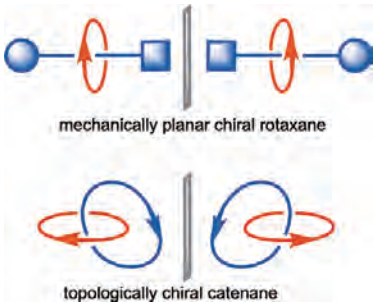

Figure 1

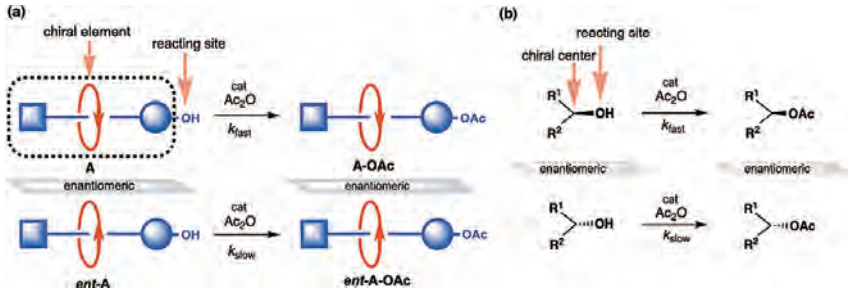

Figure 2

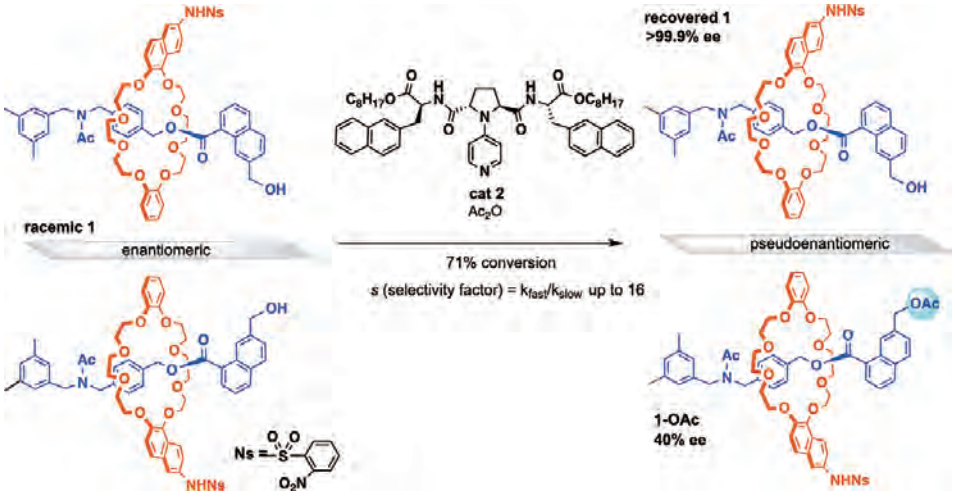

Figure 3