OIST OKINAWA INSTITUTE OF SCIENCE AND TECHNOLOGY GRADUATE UNIVERSITY

Chemistry and Chemical Bioengineering Unit (Fujie Tanaka)

FY2017 Annual Report

Chemistry and Chemical Bioengineering Unit
Professor Dr. Fujie Tanaka, Associate Professor

Abstract

The ability to design and synthesize organic molecules constitutes the foundation that underlies basic research as well as applied science. The ability is also essential for the development of pharmaceuticals and biofunctional molecules. This unit develops new, efficient, concise, and safe chemical transformation methods and strategies for constructing small molecules bearing functional groups and/or chiral centers that are relevant to the creation of biofunctional molecules. We design and create small organic molecule catalyst systems that enable designed chemical transformations, and we develop reaction strategies that use small organic molecules as enzyme-like catalysts. With the use of organic molecules as catalysts, we minimize the need for protection and deprotection steps that are usually required for the synthesis of functionalized molecules. When a reaction method does not affect functional groups that are not at the reaction site, the reaction method can be used for the synthesis of a series of molecules bearing various functional groups. This means that a series of molecules of interest may be synthesized using the same method in a short route, providing advantages for the synthesis of biofunctional candidate molecules. We also investigate the chemical bases of the reactions to understand the mechanisms of the catalysis and molecular interactions provided by organic molecules. By taking advantage of the use of features of our developing molecules, we also develop strategies and methods for conjugation of proteins and peptides with other molecules. The molecules that we have synthesized are screened in various functional assays in collaboration with other research groups. The research undertaken by this unit advances the chemistry of catalysis and of molecular synthesis. The studies by this unit accelerate the creation of molecules used in biomedical research and contribute to the development of new therapeutics, therapeutic strategies, and diagnostic methods.

1. Staff

- Dr. Ravindra D. Aher
- Dr. Avik Kumar Bagdi
- Dr. Venkati Bethi
- Dr. Santosh Chavan
- Dr. Yuvraj Garg
- Dr. Yarkali Krishna
- Dr. Lingaiah Maram
- Dr. Prodip M. Roy
- Dr. Muhammad Sohail

- Dr. Feng Yin
- Renuka Mariserla
- Kola Shilpa
- Dr. Dongxin Zhang, Graduate Student
- Tsung-Yen Huang, Graduate Student (Rotation)
- Soumen Jana, Graduate Student (Rotation)
- Deolka Shubham, Graduate Student (Rotation)
- Souvik Ghosh, Research Intern
- Maira Pasha, Research Intern
- Shiho Chinen, Research Unit Administrator

2. Activities and Findings

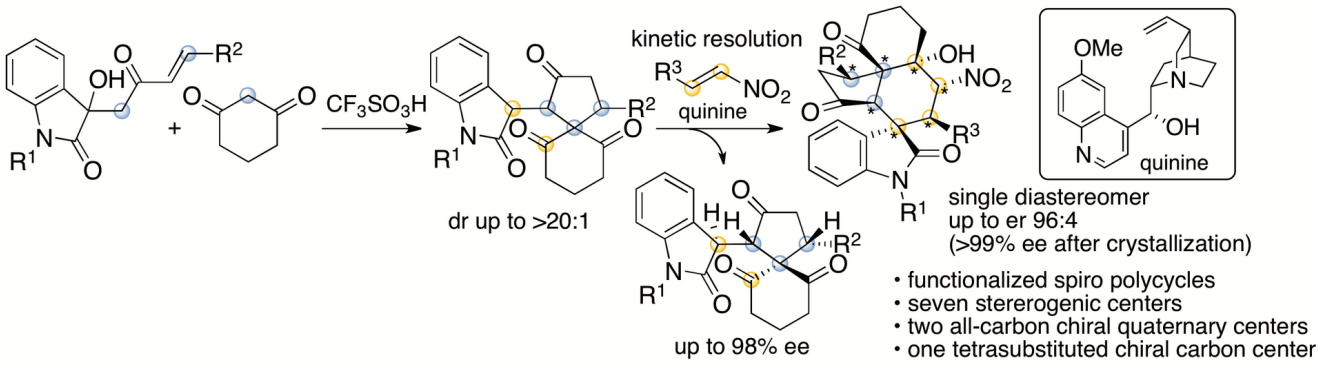
2.1. Development of new chemical transformation methods and synthesis of functionalized molecules

We have been developing small organic molecule catalysts (organocatalysts) and organocatalytic molecular transformation methods useful for the synthesis of functionalized molecules under mild conditions in short routes. We also investigate the chemical bases of the catalyses and the chemical transformations to understand the mechanisms of the catalysis and molecular interactions provided by organic molecules to further the creation of useful molecules.

Traditional synthetic methods often require high or very low temperatures and/or absolute conditions. In addition, functional groups on substrate molecules must be protected prior to reactions. That is, depending on functional groups present in target molecules to be synthesized, synthetic routes, including protection and deprotection steps, have to be designed for each molecule. To concisely synthesize functionalized molecules, chemical transformation methods that are not affected by functional groups presenting in starting materials are needed. It is a great advantage when the same reaction method can be used for the synthesis of a series of molecules bearing various functional groups without the need of product-specific protection and deprotection steps. In addition, it is desired that such reactions can be performed under safe, mild, and environmentally benign conditions. We address these points in our research as we design and develop catalysts and chemical transformation methods. By using organic molecules as catalysts, we concisely synthesize novel functionalized molecules including those that are often difficult to synthesize by traditional synthetic strategies. Our studies provide molecules that are screened for bioactive candidates and contribute to the creation of new functional molecules. Our investigations into the chemical basis of the developed catalysts and chemical transformation methods further the understanding of the chemistry of organic molecules and their reactions.

2.1.1. Asymmetric construction of spirooxindole polycycles

One of our recent achievements is the development of formal (4+1) cycloaddition and enantioselective Michael-Henry cascade reactions that provide spirooxindole polycycles (Scheme 1) (Huang, Sohail, Taniguchi, Monde, and Tanaka, *Angew. Chem. Int. Ed.* 2017, 56, 5853). Spiro[4,5]decanes and polycyclic compounds bearing spiro[4,5]decane systems are found in bioactive natural products. Functionalized molecules with these cyclic systems should be useful in drug discovery efforts.



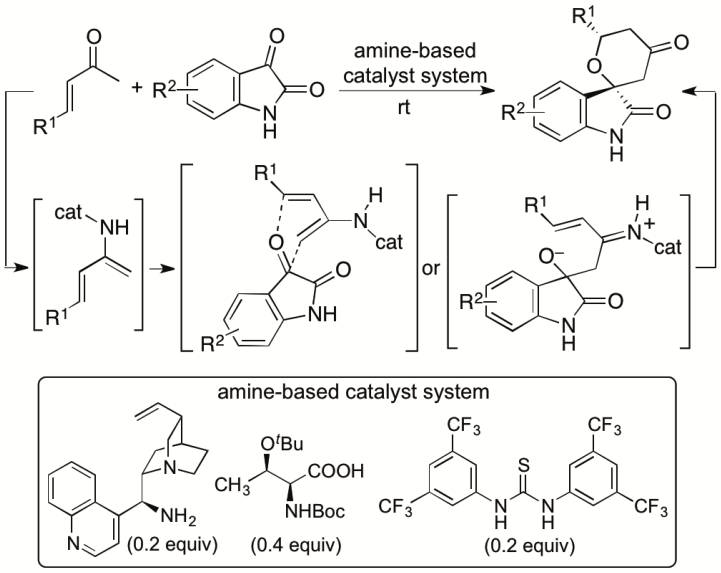
Scheme 1

We have developed formal (4+1) cycloaddition reactions that afford spiro[4,5]decane derivatives bearing oxindole moieties. We have also developed diastereo- and enantioselective Michael-Henry-cascade reactions of the (4+1) cycloaddition products that afford spirooxindole polycyclic derivatives bearing the spiro[4,5]decane system with seven stereogenic centers, including two all-carbon chiral quaternary centers and one tetrasubstituted chiral carbon center. Our strategies allow access to these complex functionalized molecules in highly enantiomerically enriched forms in two steps.

We are currently investigating the mechanisms of the formal (4+1) cycloaddition reaction that provides the spiro[4,5]decane ring system. We are also investigating the mechanisms of the reactions of the spiro[4,5]decane derivatives and expanding the capabilities for the synthesis of functionalized molecules with polycyclic ring systems.

2.1.2. Asymmetric oxa-hetero-Diels-Alder reactions: Synthesis of spirooxindole tetrahydropyran derivatives

We recently reported catalytic asymmetric hetero-Diels-Alder reactions of enones with isatins (2,3-dioxyindoles or 2,3-dioxyindolins) that provide functionalized spirooxindole tetrahydropyranones with high diastereo- and enantioselectivities (Scheme 2) (Cui and Tanaka, *Chem. Eur. J.* 2013, 19, 6213). Novel amine-based catalyst systems composed of three-types of molecules (amine, acid, and thiourea) were developed to catalyze the reactions. The design and synthesis of single-molecule catalysts that provide all the required interactions for the catalysis and stereocontrol for designed reactions especially for new reactions are often difficult. We have demonstrated that the use of multicomponent catalyst systems provides a way to bypass the limitations in the access to efficient single component catalysts. We also elucidated the mechanism of the reactions and key factors for the high diastero- and enantioselectivities achieved by the three-component catalyst system (Cui, Chouthaiwale, Yin, and Tanaka, *Asian J. Org. Chem.* 2016, 5, 153).

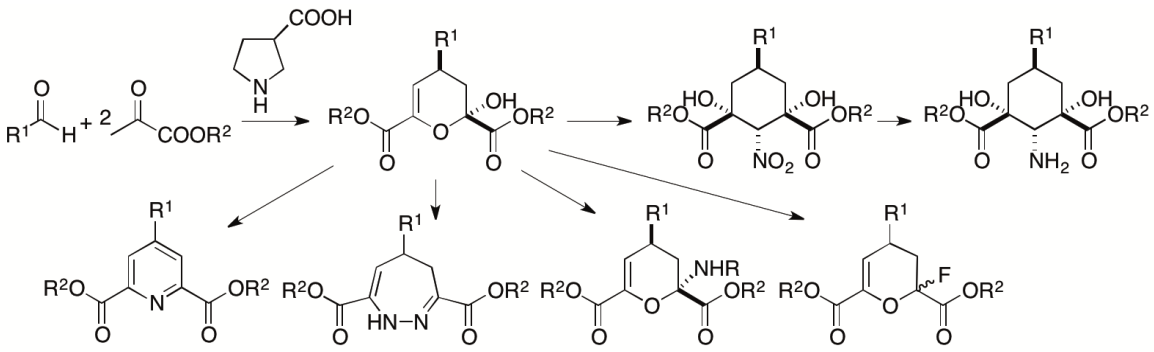


Scheme 2

With the developed reaction method and with derivatization of the hetero-Diels-Alder reaction products, various spirooxindole tetrahydropyranone derivatives were synthesized (Cui, Chouthaiwale, Yin, and Tanaka, *Org. Biomol. Chem.* 2016, 14, 259). In collaboration with Professor Tomoda, Kitasato University, SOAT2 inhibitors were identified from the synthesized spirooxindole tetrahydropyranone derivatives (Kobayashi, Ohshiro, Tomoda, Yin, Cui, Chouthaiwale, and Tanaka, *Bioorg. Med. Chem. Lett.* 2016, 26, 5899). We are investigating to expand the ability to provide biofunctional molecules through the use of the spirooxindole tetrahydropyranone structure obtained from the hetero-Diels-Alder reactions and derivatizations of the products. We are also expanding the hetero-Diels-Alder reactions of enones beyond the use of the oxindole dienophiles to the use of various ketones and aldehydes as dienophiles.

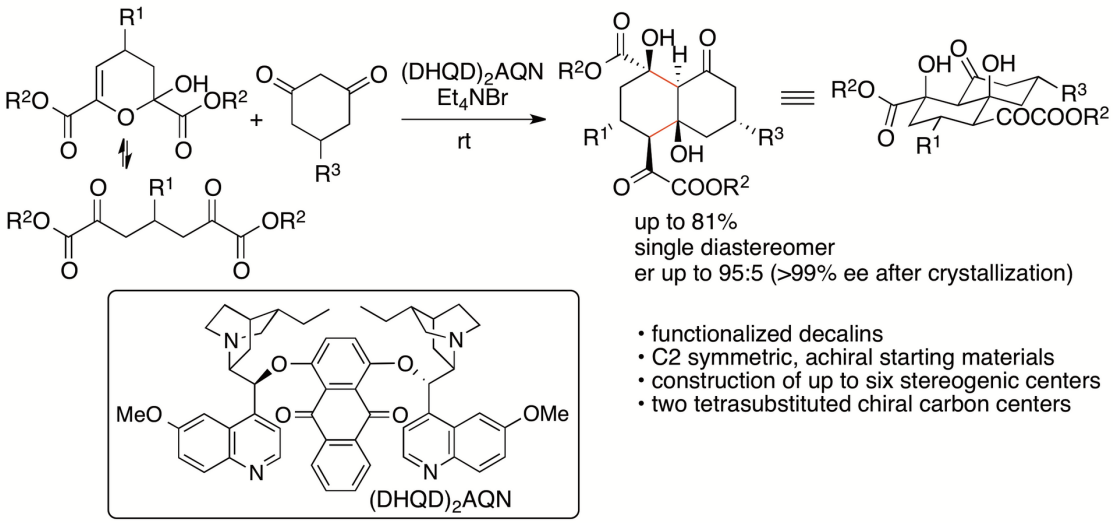
2.1.3. Reactions of pyruvates to synthesize various functionalized molecules

Pyruvates can act as nucleophiles and electrophiles and thus are expected to be useful synthons. However, the dual reactivities of pyruvates are difficult to control. We have recently developed concise cascade reactions of pyruvates to provide various functionalized dihydropyrans in one pot under mild conditions (Scheme 3) (Chouthaiwale and Tanaka, *Chem. Commun.* 2014, 50, 14881). Further, we have demonstrated that the product dihydropyrans are readily transformed to various molecules including amino group-substituted and fluoro group-substituted dihydropyrans, cyclohexane-derived amino acids, dihydrodiazepines, and pyridines. To further simplify the synthesis, we have developed a one-pot method; 4-substituted-pyridine-2,6-dicarboxylic acid derivatives were synthesized in one pot from pyruvates and aldehydes (Chouthaiwale, Lapointe, and Tanaka, *Heterocycles* 2017, 95, 587). We have also synthesized furopyrans and related derivatives from the dihydropyrans (Chouthaiwale, Aher, and Tanaka, *Heterocycles*, doi: 10.3987/COM-18-S(T)29).



Scheme 3

The dihydropyrans obtained from pyruvates and aldehydes by our method retain the a-keto ester groups of pyruvates and are C2 symmetric molecules. Taking advantage of the features of the dihydropyrans, we have developed catalytic enantioselective formal (4+2) cycloaddition via aldol-aldol annulation reactions of the dihydropyrans with cyclohexane-1,3-diones that afford functionalized decalins (Scheme 4) (Chouthaiwale, Aher, and Tanaka, *Angew. Chem. Int. Ed.* doi: 10.1002/anie.201808219). Polyfunctionalized decalins bearing five to six chiral carbon centers were obtained as single diastereomers with high enantioselectivities. Our strategy enabled the construction of five to six stereogenic centers from achiral molecules in a single transformation that formed two C-C bonds. We are investigating the mechanism of the reaction that gives the products as single diastereomers with high enantioselectivities.



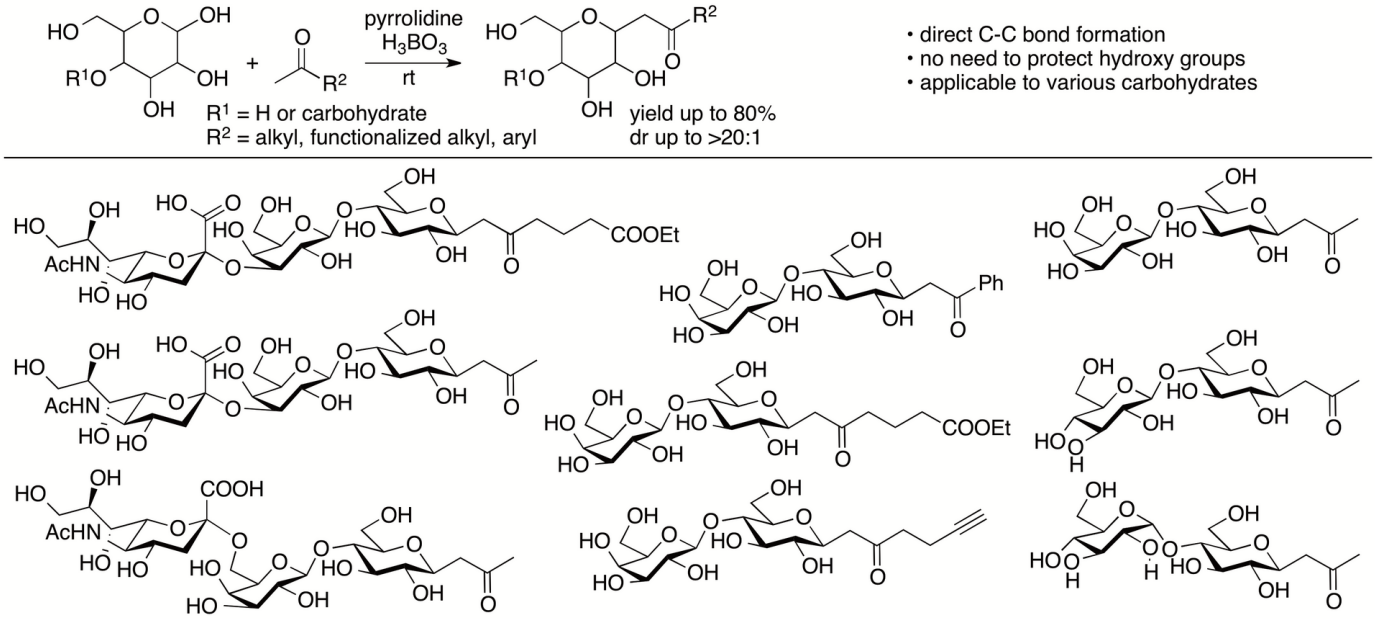
Scheme 4

We are further developing transformation methods that use the dihydropyrans obtained from pyruvates and aldehydes to concisely provide enantiomerically enriched, polyfunctionalized molecules by taming the reactivities of pyruvate derivatives.

2.1.4. Direct C-C bond-forming reactions of unprotected carbohydrates

Carbohydrate backbone-elongation reactions at anomeric carbons are important for the synthesis of higher carbon-backbone carbohydrates and of C-glycosides. Generally, reactions on carbohydrates require protection of hydroxy groups that are later deprotected. By considering atom- and step-economy, direct reactions on unprotected carbohydrates are preferable relative to the reactions requiring protection and deprotection steps

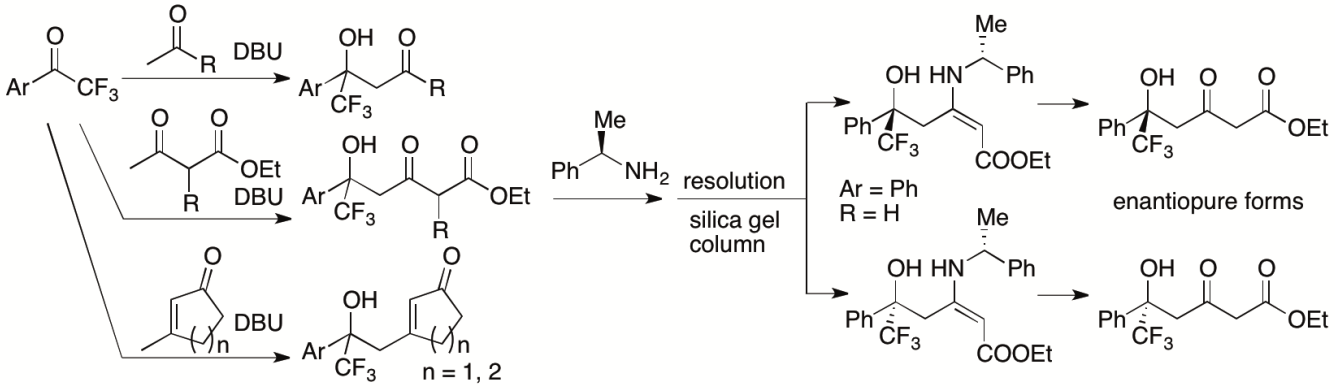
and/or strategies requiring the synthesis of preactivated forms for the reactions. There are only limited numbers of non-enzymatic direct C-C bond forming reactions at the anomeric carbon of unprotected aldoses that are mainly present as cyclic hemiacetals. We have developed direct C-glycosidation reactions of unprotected aldopyranoses with ketones including the reactions of di- and trisaccharides (Scheme 5) (Johnson, Bagdi, and Tanaka, *J. Org. Chem.* 2018, 83, 4581; Enukonda, Johnson, and Tanaka, *Heterocycles*, doi: 10.3987/COM-18-S(F)13). We are continuing to develop carbohydrate backbone-elongation reactions of unprotected carbohydrates.



Scheme 5

2.1.5. DBU-catalyzed aldol and other reactions

We have recently developed DBU-catalyzed aldol reactions that provide desired products with notable regioselectivities (Zhang, Johnson, Cui, and Tanaka, *Asian J. Org. Chem.* 2014, 3, 391; Zhang and Tanaka, *Adv. Synth. Catal.* 2015, 357, 3458). In these DBU-catalyzed aldol reactions, the C-C bonds formed in perfect regioselectivities at the methyl groups of alkyl methyl ketones, at the γ-positions of β-keto esters, and at the methyl groups of the β-methyl-substituted cyclic enones (Scheme 6). For the aldol products from the β-keto esters, enantiomerically pure forms were obtained by the resolution of the enamines of the aldol products with a homochiral amine. Using the obtained enantiomerically pure forms of the aldol products derived from the β-keto esters, we have also shown that enantiomers of chiral primary amines are concisely detected by ^{1}H NMR through the formation of the enamines with the aldol products (Zhang, Chuang, Cao, Krishna, Shilpa, and Tanaka, *Tetrahedron Letter*, 2018, 59, 2248). With this detection method by ^{1}H NMR analyses, determination of enantiomer ratios of the amines, including those that have the chiral centers at positions remote from the amine groups, was also possible. The DBU-catalyzed aldol reactions allowed the access to the aldol products useful for various purposes.

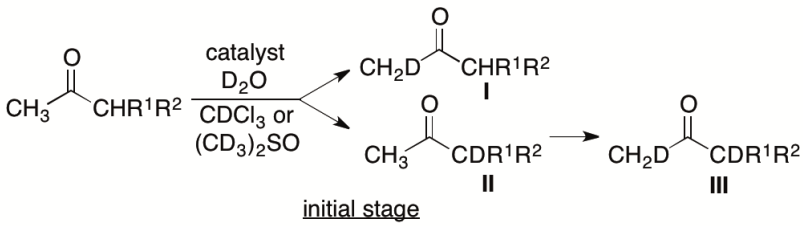


Scheme 6

As a next stage, we are designing and synthesizing DBU-inspired chiral versions of catalysts to perform enantioselective aldol reactions and related reactions. We are also developing DBU-catalyzed Mannich reactions and other reactions.

2.1.6. Mechanisms of the catalysis and regioselectivities of aldol reactions

As described above, we have shown that the DBU catalysis provides notable regioselectivities in aldol reactions. In the catalyzed reactions of ketones, the relationship between the formation of enolates or enamines and the formation of products, including regioselective formation of products, is not well understood. When a ketone has two enolizable α-positions, the carbanion may form at both the α-positions or at either of the α-positions. Regioselectivities of catalyzed aldol and related reactions may be the results of regioselective formation of an enolate/enamine or because a single type of enolates/enamines among those formed results in product formation. To provide insight into aldol reaction catalysis, the relative frequencies of carbanion formation at each a-position of ketones under catalysis by DBU, proline, and related catalysts were determined through the deuteration of the ketones in the presence of these catalysts (Scheme 7) (Zhang and Tanaka, *Org. Lett.* 2017, 19, 3803). For the reaction of 1,1-dimethoxypropan-2-one, the deuterated site matched the C-C bond formation site in the aldol reactions, and faster reaction by the DBU catalysis than that by proline catalysis was in accord with the faster deuteration rate by DBU than that by proline catalysis. For other ketones tested in this study, such as 2-pentanone, methoxyacetone, hydroxyacetone, and ethyl 3-oxobutanoate, however, the positions favored for deuteration did not directly correlate with the C-C bond formation sites in aldol and related reactions. Formation of carbanions (or enolates/enamines) is necessary to be the reaction site, and for fast reactions, rapid or frequent enolate/enamine formation is required. But, the results indicate that frequent carbanion formation site is not necessary to be the C-C bond formation site. Through this study, mechanisms of regioselectivities of the reactions and mechanisms of catalysis were clarified to some degree.



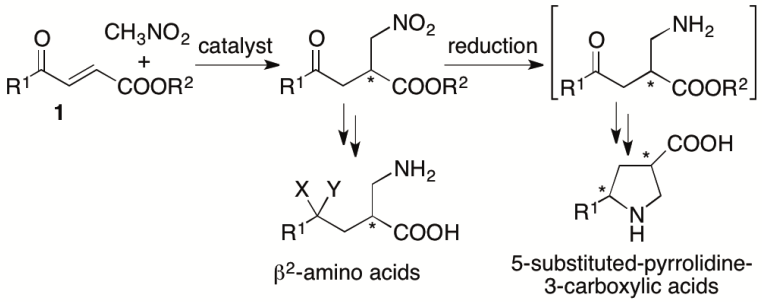
initial stage

$R^1 = R^2 = OCH_3$	**I** only (DBU, proline, or β-proline)
$R^1 = CH_3$, $R^2 = H$	**I** and **II** (DBU, proline, or β-proline)
$R^1 = OCH_3$, $R^2 = H$	**I** > **II** (DBU, proline, or β-proline)
$R^1 = OH$, $R^2 = H$	**I** > **II** (DBU, β-proline), **I** >> **II** (proline)
$R^1 = CO_2C_2H_5$, $R^2 = H$	**II** (R^2 = D) then **III** (R^2 = D) (DBU)

Scheme 7

2.1.7. Asymmetric Michael reactions: Synthesis of pyrrolidine-3-carboxylic acid derivatives

Pyrrolidine-3-carboxylic acid (β-proline) derivatives and β^2-amino acids are important molecules as bioactives, catalysts for chemical transformations, and their building blocks. To concisely synthesize these compounds, we have developed organocatalytic enantioselective Michael reactions of 4-alkyl-substituted-4-oxo-2-enoates with nitroalkanes (Scheme 8) (Yin, Garifullina, and Tanaka, *Org. Biomol. Chem.* 2017, 15, 6089; Yin, Garifullina, and Tanaka, *Org. Biomol. Chem.* 2018, 16, 3052). Using the developed method, highly enantiomerically enriched 5-methylpyrrolidine-3-carboxylic acid was synthesized in two steps from easily accessible starting materials.



Scheme 8

2.2. Fluorescence-based reaction monitoring systems

We have been developing concise fluorescence-based assay methods to monitor bond-forming and bond-breaking reaction progress on a small scale to facilitate the development of catalysts and catalyzed chemical transformation methods. Use of fluorogenic substrates provides a straightforward method of reaction monitoring because reaction progress is directly observed as an increase in fluorescence.

For example, we have developed fluorogenic aldehydes based on a diarylacetylene core structure and fluorescence-based assay systems for aldol reactions using the fluorogenic aldehydes (Katsuyama, Chouthaiwale, Akama, Cui and Tanaka, *Tetrahedron Lett.* 2014, 55, 74). We are continuing to develop fluorogenic substrates and fluorescence-based assay systems with improved features.

2.3. Development of bioconjugation systems

Protein labeling methods are required for the synthesis of antibody-drug conjugates and other protein conjugates; these molecules are important as therapeutics and as detection devices for molecules of interest. Conjugation reactions are also needed to create multifunctional molecules. We are developing efficient protein labeling systems and molecules with desired reactivities that can be used for protein labeling reactions at targeted sites.

2.4. Search of biofunctional molecules

As described above, we have synthesized various functionalized molecules. In collaboration with researchers whose expertise is in biology and screening for biofunctional molecules, we have been searching new

biofunctional molecules and drug leads. The collaborations include:

• Professor Hiroshi Tomoda, Kitasato University

3. Publications

3.1 Journals

1. Chouthaiwale, P. V.; Lapointe, S.; Tanaka, F. Synthesis of 4-substituted-pyridine-2,6-dicarboxylic acid derivatives from pyruvates and aldehydes in one pot. *Heterocycles*, 95, 587-594 (2017), doi: 10.3987/COM-16-S(S)27.
2. Huang, J.-R.; Sohail; M.; Taniguchi, T.; Monde, K.; Tanaka, F. Formal (4+1) cycloaddition and enantioselective Michael-Henry-cascade reactions to synthesize spiro[4,5]decanes and spirooxindole polycycles. *Angewandte Chemie Internal Edition*, 56, 5853-5857 (2017), doi: 10.1002/anie.201701049. *Angewandte Chemie*, 129, 5947-5951 (2017), doi: 10.1002/ange.201701049.
3. Zhang, D.; Tanaka, F. Determination of relative frequency of carbanion formation at a-positions of ketones under aldol reaction catalysis conditions. *Organic Letters* 19, 3803-3806 (2017), doi: 10.1021/acs.odglett.7b01676.
4. Yin, F.; Garifullina, A.; Tanaka, F. Synthesis of pyrrolidine-3-carboxylic acid derivatives via asymmetric Michael addition reactions of carboxylate-substituted enones. *Organic & Biomolecular Chemistry* 15, 6089-6092 (2017), doi: 10.1039/c7ob01484h.
5. Yin, F.; Garifullina, A.; Tanaka, F. Correction: Synthesis of pyrrolidine-3-carboxylic acid derivatives via asymmetric Michael addition reactions of carboxylate-substituted enones. *Organic & Biomolecular Chemistry* 16, 3052-3053 (2018), doi: 10.1039/c8ob90051e.
6. Chouthaiwale, P. V.; Aher, R. D.; Tanaka, F. Reactions of pyruvate-derived dihydropyrans with formaldehyde: synthesis of functionalized furopyrans and related products. *Heterocycles* 97, in press (2018), doi: 10.3987/COM-18-S(T)29.
7. Johnson, S.; Bagdi, A. K.; Tanaka, F. C-Glycosidation of unprotected di- and trisaccharide aldopyranoses with ketones using pyrrolidine-boric acid catalysis. *The Journal of Organic Chemistry*, 83, 4581-4597 (2018), doi: 10.1021/acs.joc.8b00340.
8. Zhang, D.; Chuang, P.-S.; Cao, D.; Krishna, Y.; Shilpa, K.; Tanaka, F. Detection of enantiomers of chiral primary amines by ^{1}H NMR analysis via enamine formation with an enantiopure γ-position aldol product of a β-keto ester. *Tetrahedron Letters*, 59, 2248-2250 (2018) doi: 10.1016/j.tetlet.2018.04.079.
9. Enukonda, J.; Johnson, S.; Tanaka, F. C-Glycosidation of unprotected aldopentoses with ketones using proline-triethylamine as catalyst. *Heterocycles* 99, in press (2018) doi: 10.3987/COM-18-S(F)13.
10. Chouthaiwale, P. V.; Aher, R. D.; Tanaka, F. Catalytic enantioselective formal (4+2) cycloaddition by aldol-aldol annulation of pyruvate derivatives with cyclohexane-1,3-diones to afford functionalized decalins. *Angewandte Chemie Internal Edition*, in press (2018), doi: 10.1002/anie.201808219. *Angewandte Chemie*, in press, doi: 10.1002/ange.201808219.

3.2. Oral and Poster Presentations

1. Zhang, D.; Tanaka, F. DBU-catalyzed regioselective aldol reactions to synthesize functionalized molecules, in The 45th ACS National Organic Chemistry Symposium (NOS 2017), UC Davis, US, 2017.06.25-2017.06.29. (poster No. W56)

2. Maram, L.; Tanaka, F. Stereoselective synthesis of iminosugar C- glycosides via a Mannich-aminocyclization route, in Chirality 2017; 29th International Symposium on Chirality, Tokyo, Japan, 2017.07.09-2017.07.12. (poster No. P-130)
3. Sohail, M.; Huang, J.-R.; Tanaka, F. Enantioselective synthesis of functionalized spiro[4,5]decanes and spirooxindole polycycles by formal (4+1) cycloaddition and Michael Henry-cascade reactions, in Chirality 2017; 29th International Symposium on Chirality, Tokyo, Japan, 2017.07.09-2017.07.12. (poster No. P-132)
4. Sohail, M.; Huang, J.-R.; Tanaka, F. Two steps, (4+1) cycloaddition and kinetic resolution by Michael Henry-cascade reactions, leading to highly functionalized enantiomerically enriched spiro[4,5]decanes and spirooxindole polycycles, in the 254th ACS National Meeting, Washington, DC, US, 2017.08.20-2017.08.24. (oral presentation No. ORGN 488)
5. Aher R., Chouthaiwale P.; Tanaka, F. Organocatalytic enantioselective synthesis of functionalised decalines *via* formal [4+2] cycloaddition of substituted dihydropyrans and 1,3-diketones, in The 10th Symposium on Organocatalysis, Sendai, Japan, 2017.11.30-2017.12.01. (poster No. P18)
6. Sohail, M.; Huang, J.-R.; Tanaka, F. Two steps, formal (4+1) cycloaddition and enantioselective Michael-Henry cascade reactions, leading to highly functionalized spiro[4,5]decanes and spirooxindole polycycles, in The 10th Symposium on Organocatalysis, Sendai, Japan, 2017.11.30-2017.12.01. (poster No. P31)
7. Oka, M.; Inaba, S.; Numoto, N.; Ito, N.; Roy, P. K.; Tanaka, F.; Oda, M. Determination and analyses of structures and functions of designer aldolase RA61 using the mutants, in The 2018 Annual Meeting of The Japan Society for Bioscience, Biotechnology and Agrochemistry, Nagoya, Japan, 2018.03.15-2018.03.18.
8. Krishna, Y.; Tanaka, F. Catalytic intramolecular Mannich reaction of hydroxylactam-enals for access to bicyclic N-heterocycles, in The 138th Annual Meeting of the Pharmaceutical Society of Japan, Sendai, Japan, 2018.03.25-2018.03.28. (poster No. 27PA-am053)
9. Maram, L.; Tanaka, F. Stereoselective synthesis of iminosugar C-glycosides via a Mannich-aminocyclization reactions, in The 138th Annual Meeting of the Pharmaceutical Society of Japan, Sendai, Japan, 2018.03.25-2018.03.28. (poster No. 27PA-pm046)
10. Tanaka, F. Generation of ketone nucleophiles and their reactions: Activation of substrates and control of reactions using organic molecules, in the class of Division of Chemistry, Graduate School of Science, Kyoto University, Kyoto, Japan, 2018.06.05. (invited, oral)

4. Intellectual Property Rights

1. Tanaka, F.; Yin, F. Concise process for preparing 3-pyrrolidine carboxylic acid derivatives, PCT/JP2016/004377, WO/2018/025295 (publication date 2018.02.08).

5. Other Activities

5.1. OIST internal seminar

- Sohail, M
- OIST internal seminar
- Synthesis of complex functionalized molecules: spiro[4,5]decanes and spirooxindole polycycles

- Date: November 10, 2017

6. Seminars Hosted

- Date: April 20, 2017
- Venue: OIST campus
- Speaker: Prof. Shu Kobayashi, The University of Tokyo, Japan
- Title: Metal Nanoparticles as Novel Catalysts for Organic Synthesis

- Date: July 11, 2017
- Venue: OIST campus
- Speaker: Prof. Ikuo Fujii, Osaka Prefecture University, Japan
- Title: Post-antibody Drugs: Generation of Molecular-targeting Peptides "*MicroAntibodies*" by Directed Evolution in Phage-displayed Libraries of Conformationally Constrained Peptides

- Date: August 23, 2017
- Venue: OIST campus
- Speaker: Prof. Hisashi Yamamoto, Chubu University, Japan
- Title: Substrate Controlled Asymmetric Reactions

- Date: September 8, 2017
- Venue: OIST campus
- Speaker: Dr. Naoya Kumagai, Institute of Microbial Chemistry, Tokyo, Japan
- Title: Reaction Development in the Amide Playground

- Date: October 27, 2017
- Venue: OIST campus
- Speaker: Prof. Leiv K. Sydnes, Department of Chemistry, University of Bergen, Norway
- Title: 1,1,2,2-Tetraethoxybutyne - simple to make and exciting to use

- Date: February 7, 2018
- Venue: OIST campus
- Speaker: Prof. Magne O. Sydnes, Department of Mathematics and Natural Science, University of Stavanger, Norway
- Title: Synthesis of Natural Products and Photochemical Transformations