# 7th CCS-CSJ Young Chemists Forum 2017

## – Frontier in Organic Synthesis toward Middle Molecular Strategy –

**March 18th (Sat), 2017**

**Hiyoshi Campus, Keio University, Yokohama, Kanagawa, Japan**

**The Chemical Society of Japan & The Chinese Chemical Society**

# *Welcome to Japan!*

Dear Colleagues

Globalization is the process of international integration arising from the interchange of world views, products, ideas, and other aspects of culture.

Particularly, collaborations between chemists of various countries often transcend borders and cultural differences. The fundamental nature of chemical science allows chemists to communicate using knowledge of their field. Its focus is on chemistry students and chemists interested in developing a global approach to open new science and technology, by participating in an international symposium. Overall, multidisciplinary is the password for the successful globalization of chemistry.

The Chemical Society of Japan (CSJ) is delighted to be co-organizing with the Chinese Chemical Society (CCS) at the occasion of 97th Annual Meeting of Chemical Society of Japan at Yokohama. I am confident that multidisciplinary research can be developed through this international joint forum.

I would like to thank Prof. Biao Yu, representing CCS as Chairs, as well as Prof Koichi Fukase and Prof. Takayuki Doi, representing CSJ as Chairs, for their great effort to make CCS-CSJ young chemists' forum possible.

Mutual exchange and collaboration among chemists between two countries have continued ever after, even when the flow of knowledge became no longer one-sided, as it was in early days, and have led to tremendous contributions to the development of new chemistry.

It is our great pleasure and honor to add new pages to the history of mutual exchange between global countries.

Professor Hisashi Yamamoto

President;

The Chemical Society of Japan

**The 7th CCS-CSJ Young Chemists Forum 2017**
**—Frontier in Organic Synthesis toward Middle Molecular Strategy**
The Chemical Society of Japan The 97th Annual Meeting

■Date March 18th (Saturday), 2017 9:00-17:40
■Venue S2; Room J24, House B, Bldg. 4,
Hiyoshi Campus, Keio University, Yokohama, Kanagawa, Japan
■Hosted by The Chemical Society of Japan & The Chinese Chemical Society

| | | | |
|---|---|---|---|
| 09:00 | Opening Remarks | **Representative from CSJ**<br>**Hisashi Yamamoto**<br>President of the CSJ | |
| 09:05 | Introductory Talk | **Koichi Fukase,**<br>Osaka University | …2 |
| 09:10 | Aromatic Molecules: Decarbonylative Coupling and Multiple Arylation | **Junichiro Yamaguchi,**<br>Waseda University | …3 |
| 09:40 | C-H Functionalization Strategy for Chemical Synthesis of α-Amino Acids and Complex Peptides | **Gong Chen,**<br>Nankai University | …5 |
| 10:10 | **Coffee break** | | |
| 10:20 | Synthesis and Biological Evaluation of Antibiotic Polyketides | **Yoko Saikawa,**<br>Keio University | …7 |
| 10:50 | Natural Product Synthesis Facilitated by Ligand Design | **Wenjun Tang,**<br>Shanghai Institute of Organic Chemistry | …9 |
| 11:20 | Synthesis of Monomers for Spectomycin B1,<br>A Middle Size SUMOylation Inhibitor Molecule | **Go Hirai,**<br>Kyushu University | …11 |
| 11:50 | **Lunch** | | |
| 13:10 | Remote Activation of *O*/*S*-Benzyl Glycosides in Latent-Active Glycosylation | **Qian Wan,**<br>Huazhong Univ. of Science and Technology | …13 |
| 13:40 | Development of the Novel Cancer Immunotherapy Utilizing α-Gal | **Yoshiyuki Manabe, et al.**<br>Osaka University | …15 |
| 14:10 | Type II Intramolecular [5+2] Cycloaddition | **Chuang-Chuang Li,**<br>South Univ. of Science & Technology of China | …17 |
| 14:40 | **Coffee break** | | |
| 14:50 | Aryl Fluorides: a Versatile Synthetic Platform for Natural Product Synthesis | **Ken Ohmori,**<br>Tokyo Institute of Technology | …19 |
| 15:20 | Total Synthesis of Bioactive Natural Products: Efficiency and Diversity | **Shuanhu Gao,**<br>East China Normal University | …21 |
| 15:50 | **Coffee break** | | |
| 16:00 | Development of Chemical Assembly Lines Generating Skeletally Diverse Natural Products and Their Variants | **Hiroki Oguri,**<br>Tokyo Univ. of Agriculture and Technology | …23 |
| 16:30 | Complex Natural Product as a Driving Force for Discovery in Organic Synthesis and Chemical Biology | **Xiaoguang Lei,**<br>Peking University | …25 |
| 17:00 | **Closing Remarks** | **Representative from CCS**<br>**Biao Yu**<br>Shanghai Institute of Organic Chemistry | …13 |

# *Welcome Address*

*Dear Friends and Colleagues:*

On behalf of the Chinese chemists attending the 7th CCS (The Chinese Chemical Society)-CSJ (The Chemical Society of Japan) Joint Forum, I express my sincere gratitude to our Japanese colleagues for hosting such a wonderful event in the beautiful campus of Keio University.

This year's forum focuses on the Frontier in Organic Synthesis toward Middle Molecular Strategy. Therefore, peptides, carbohydrates, as well as the diverse natural products, covering the core space of organic molecules will be the topics. Chemical synthesis to deliver these molecules and to make the corresponding probes for deciphering their functions have always been the major tasks of organic chemists; the young colleagues form China and Japan will enjoy exchanging the new visions and new discovery.

In this complex and changing world, delivery of useful molecules and exchange of views face to face are two most valuable measures to make the would better.

I believe all the participants will enjoy the chemistry we bring together, and the cherry blossom season as well. And I wish this bilateral Forum for young chemists will continue forever.

**Professor Biao Yu**
State Key Laboratory of Bio-organic and Natural Products Chemistry, Shanghai Institute of Organic Chemistry, CAS
345 Lingling Road, Shanghai 200032, China
Tel & Fax: (+86)-21-54925131 E-mail: byu@sioc.ac.cn

## ➢ Educational Background

1989 B.Sc., Department of Technical Physics, Peking University

1995 Ph D., Shanghai Institute of Organic Chemistry, CAS (supervisor: Prof. Yongzheng Hui)

## ➢ Professional Career

1995 New York University (PD)

1996 Assistant professor, Shanghai Institute of Organic Chemistry, CAS

1997 Associate professor, Shanghai Institute of Organic Chemistry, CAS

1999 Professor, Shanghai Institute of Organic Chemistry, CAS

## ➢ Research Interests

Total synthesis, synthetic methodology, and chemical biology of carbohydrates and glycoconjugates.

## ➢ Awards

A number of awards including the National Natural Science Award (2010), the Lilly Scientific Excellence Award (2012), and Fellow of the Royal Society of Chemical (2016).

## ➢ Recent Publications

1. Total synthesis of periploside A, a unique pregnane hexasaccharide with potent immunosuppressive effects. Zhang, X.; Zhou, Y.; Zuo, J.; Yu, B. *Nature Commun.* **2015**, 6: 5879.
2. Total synthesis of nucleoside antibiotic A201A. Nie, S.; Li, W.; Yu, B. *J. Am. Chem. Soc.* **2014**, ***136,*** **4157-4160**.
3. Mechanistic insights into the gold(I)-catalyzed activation of glycosyl *ortho*-alkynylbenzoates for glycosidation. Tang, Y.; Li, J.; Zhu, Y.; Li, Y.; Yu, B. *J. Am. Chem. Soc.* **2013**, ***135,*** **18396-18405**.
4. Assembly of naturally occurring glycosides, evolved tactics and glycosylation methods. Yu, B.; Sun, J.; Yang, X. *Acc. Chem. Res.* **2012**, *45*, 1227-1236.

## Koichi Fukase

Professor
Graduate School of Science, Osaka University
Address: Machikaneyama 1-1, Toyonaka, Osaka, 560-0043, Japan
Tel: (+81) 6-6850-5388
FAX: (+81) 6-6850-5419
E-mail: koichi@chem.sci.osaka-u.ac.jp

### ➢ Educational Background

1982 B.Sci., Osaka University (supervisor: Prof. Tetsuo Shiba)
1987 Doctor of Science, Graduate School of Science, Osaka University (supervisor: Prof. Tetsuo Shiba)

### ➢ Professional Career

1987 Research Fellow of Japan Society for the Promotion of Science, Osaka University
1988 Research Associate, Graduate School of Science, Osaka University
1994-1995 Postdoctoral Fellow, Department of Chemistry, Columbia University (Professor W. Clark Still)
1996 Assistant Professor, Graduate School of Science, Osaka University
1998 Associate professor, Graduate School of Science, Osaka University
2004 Professor, Graduate School of Science, Osaka University

### ➢ Research Fields

Organic synthesis, Natural product chemistry, Bioorganic chemistry, Chemical biology, Carbohydrate chemistry, Innate immunity, Combinatorial chemistry, Molecular imaging.

### ➢ Awards

1994 The Chemical Society of Japan Award For Young Chemists
2003 BCSJ award (the best paper award of Bull. Chem. Soc. Jpn., Vol 76. March)
2008 BCSJ award (the best paper award of Bull. Chem. Soc. Jpn., Vol 81. July)
2009 Dohgane Award, which is given to a researcher who made significant contribution to the field of automated flow and microreactor (Group for Research on Automated Flow and Microreactor Synthesis, Kinki Chemical Society, Japan)
2011 The Chemical Society of Japan Award for Creative Work

### ➢ Recent Publications

1. "Synthesis of peptidoglycan fragments from *Enterococcus faecalis* with Fmoc-strategy for glycan elongation", N. Wang, H. Hasegawa, CY. Huang, K. Fukase, and Y. Fujimoto, *Chem. Asian J.* **2017**, 12, 27-30.
2. "Chemical synthesis of a complex-type *N*-glycan containing a core fucose", M. Nagasaki, Y. Manabe, N. Minamoto, K. Tanaka, S. Silipo, S. Molinaro, and K. Fukase, *J. Org. Chem.* **2016**, *81*, 10600-10616.
3. "A reduction-based sensor for acrolein conjugates with the inexpensive nitrobenzene as an alternative to monoclonal antibody" M. Takamatsu, K. Fukase, R. Oka, S. Kitazume, N. Taniguchi, and K. Tanaka K. *Sci. Rep.* **2016**, *6*, 35872.
4. "Efficient synthesis of the disialylated tetrasaccharide motif in N-glycans through an amide-protection strategy." J. Zhou, Y. Manabe, K. Tanaka, and K. Fukase, *Chem. Asian J.* **2016**, *11*, 1436-1440.

## Junichiro Yamaguchi

**Associate Professor**
Faculty of Science and Engineering, Waseda University
3-4-1 Ohkubo, Shinjuku, Tokyo 169-8555, Japan
Phone: +81-3-5286-3225
E-mail: junyamaguchi@waseda.jp

### ➢ Educational Background

2002 B.Sc. Tokyo University of Science, Japan (supervisor: Prof. Yujiro Hayashi)
2004 M.Sc. Graduate School of Engineering, Tokyo University of Science, Japan (supervisor: Prof. Yujiro Hayashi)
2006 Exchange Student, The Scripps Research Institute, USA (Prof. K. C. Nicolaou)
2007 Doctor of Engineering, Graduate School of Engineering, Tokyo University of Science, Japan (supervisor: Prof. Yujiro Hayashi)

### ➢ Professional Career

2007 Postdoctoral Researcher, The Scripps Research Institute, USA (with Professor. Phil S. Baran)
2008 Assistant Professor, Graduate School of Science, Nagoya University, Japan (with Professor Kenichiro Itami)
2012 Associate Professor, Graduate School of Science, Nagoya University, Japan
2016 Associate Professor (PI), Faculty of Science and Engineering, Waseda University, Japan

### ➢ Research Interests

1) Organic synthesis
2) Synthesis of natural products

### ➢ Awards

2009 Teijin Pharma Award in Synthetic Organic Chemistry, Japan
2011 Young Scientist's Research Award in Natural Product Chemistry, Japan
2012 The Chemical Society of Japan Lecture Award for Young Chemists
2013 Japan Union of Chemical Science and Technology Chemistry Communication Award
2013 The Chemical Society of Japan Award for Distinguished Young Chemists
2014 Banyu Chemist Award
2014 Thieme Chemistry Journal Award
2014 Asian Core Lectureship Award, China and Thailand

### ➢ Recent Publications

1. "Toward an Ideal Synthesis of (Bio)molecules through Direct Arene Assembling Reactions" (Accounts), Yamaguchi, J.; Itami, K. *Bull. Chem. Soc. Jpn.* **2017** DOI: 10.1246/bcsj.20160365.
2. "Decarbonylative Organoboron Cross-coupling of Eters by Nckel Catalysis" Muto K.; Yamguchi, J.; Musaev, D. G.; Itami, K. *Nature. Commun.* **2015**, *6*, 7508.
3. "Synthesis and Characterization of Hexaarylbenzenes with Five or Six Different Substituents Enabled by Programmed Synthesis", Suzuki, S.; Segawa, Y.; Itami, K.; Yamaguchi, J. *Nature Chem.* **2015**, *7*, 227.
4. "Concise Syntheses of Dictyodendrins A and F by a Sequential C−H Functionalization Strategy", Yamaguchi, A.; Chepiga, K.; Yamaguchi, J.; Itami, K.; Davies, H. *J. Am. Chem. Soc.* **2015**, *137*, 644.

# Aromatic Molecules: Decarbonylative Coupling and Multiple Arylation

Junichiro Yamaguchi
*Department of Applied Chemistry, Waseda University,*
*3-4-1 Ohkubo, Shinjuku, Tokyo 169-8555, Japan*

In recent years, catalytic decarbonylative coupling reactions using aromatic esters as aryl electrophiles have been studied to produce various transformations. We report the development of catalytic decarbonylative transformations of aromatic esters, which are C–H arylation of azoles, Suzuki–Miyaura coupling, alkynylation, and intramolecular etherifications under the influence of Pd or Ni catalysts. The key for these achievements was newly developed catalytic systems in which our unique ligand was employed (Figure 1A). By utilization of these reactions, we successfully achieved applications such as the formal synthesis of naturally occurring compounds.

Meanwhile, multiply arylated aromatics have often been found in natural products, pharmaceuticals and functional organic materials. We achieved the programmed synthesis of multiply arylated aromatics using sequential C–H couplings, cross couplings, and Diels–Alder reaction of thiophene S-oxides. This synthetic method can provide hexaarylbenzenes, pentaarylpyridines, multiply arylated naphthalenes, and a multiply arylated anthracene bearing different aryl groups (Figure 1B).

I would like to talk about above two topics about transformation of aromatic molecules in this symposium.

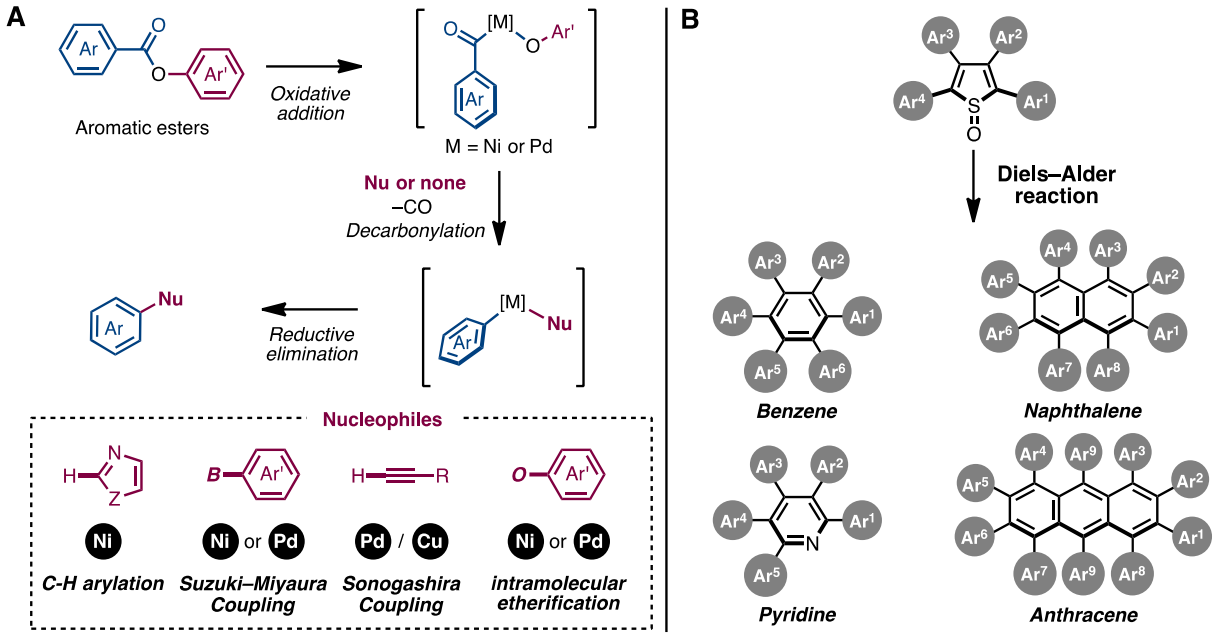



**Figure 1.**

## Gong Chen

Professor of Chemistry
State Key Laboratory of Elemento-Organic Chemistry
Nankai University
Address: Weijin Rd 94, Tianjin 300071, China
Tel & Fax: (+86)-22-8366-2300
E-mail: gongchen@nankai.edu.cn

### ➢ Educational Background

1998 B.Sc., Nanjing University
2004 Ph.D., Department of Chemistry, Columbia University (supervisor: Prof. Dalibor Sames)

### ➢ Professional Career

2005 Memorial Sloan-Kettering Cancer Center (Postdoc)
2008 Assistant professor, The Pennsylvania State University
2014 Associate professor, The Pennsylvania State University
2015 Professor, Nankai University

### ➢ Research Interests

1) Synthesis of complex peptides and carbohydrates
2) C-H Functionalization

### ➢ Awards

2011 National Science Foundation CAREER Award
2013 Amgen Young Investigator
2016 WuXi AppTec Scholar Award in Life Science and Chemistry

### ➢ Recent Publications

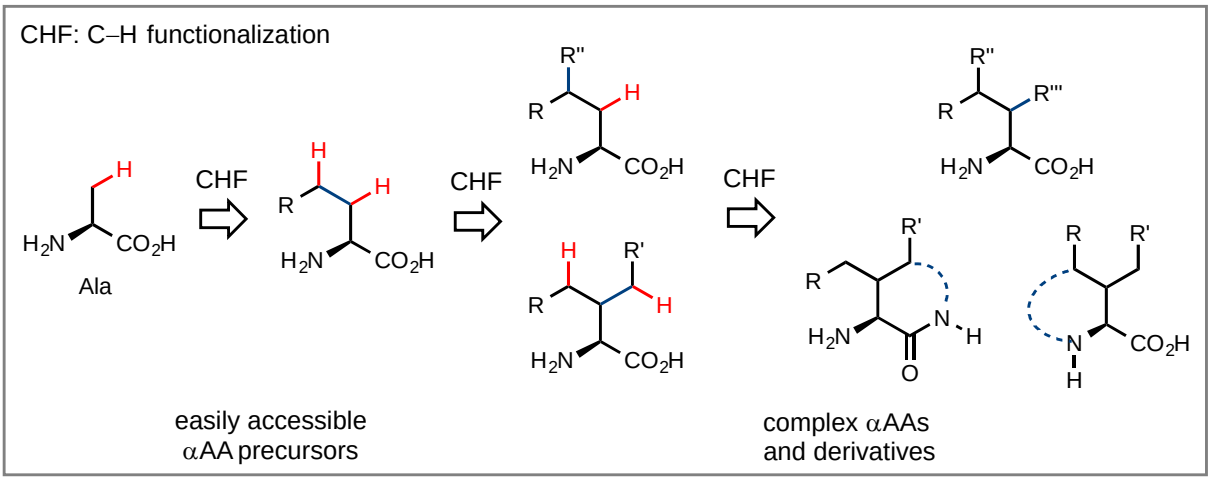
1. "Total Synthesis of Celogentin C via Stereoselective C−H Activation", Yiqing Feng and Gong Chen. *Angew. Chem., Int. Ed.* **2010**, *49*, 958-961.
2. "Syntheses and Transformations of α-Amino Acids via Palladium-Catalyzed Auxiliary-Directed $sp^3$ C−H Functionalization", Gang He, Bo Wang, William A Nack, and Gong Chen. *Acc. Chem. Res.* **2016**, *49*, 635-645.
3. "Benzazetidine Synthesis via Palladium-Catalyzed Intramolecular C−H Amination ", Gang He, Gang Lu, Zhengwei Guo, Peng Liu, and Gong Chen. *Nature Chem.* **2016**, *8*, 1131-1136.
4. "Total Synthesis of Mannopeptimycins α and β", Bo Wang, Yunpeng Liu, Rui Jiao, Yiqing Feng, Qiong Li, Chen Chen, Long Liu, Gang He, and Gong Chen. *J. Am. Chem. Soc.* **2016**, *138*, 3926-3932.

# C−H Functionalization Strategy for Chemical Synthesis of α-Amino Acids and Complex Peptides

Gong Chen

*State Key Laboratory of Elemento-Organic Chemistry, Nankai University, Tianjin, 300071, P. R. China*

α-Amino acids (αAA) are one of the most useful chiral building blocks for synthesis. Despite significant advances in synthetic methodology, the efficient synthesis of enantiopure αAAs carrying complex side chains, as seen in numerous peptide natural products, remains challenging. Complementary to the conventional synthetic strategies, a strategy based on the selective functionalization of side chain C−H bonds, particularly $sp^3$ hybridized C−H bonds, of various readily available αAA precursors may provide a more straightforward and broadly applicable means for the synthesis and transformation of αAAs. Over the past few years, we have carried out systematic investigation of palladium-catalyzed bidentate auxiliary-directed C−H functionalization reactions for αAA substrates. Our strategies utilize two different types of amide-linked auxiliary groups, attached at the *N* or *C* terminus of αAA substrates, to exert complimentary regio- and stereo-control on C−H functionalization reactions through palladacycle intermediates. A variety of αAA precursors can undergo multiple modes of $C(sp^3)$−H functionalization, including arylation, alkenylation, alkynylation, alkylation, alkoxylation and intramolecular aminations, at the β, γ and even δ positions to form new αAA products with diverse structures. In addition to transforming αAAs at previously unreachable positions, these palladium-catalyzed C−H functionalization strategies enable new retrosynthetic logic for the synthesis of many basic αAAs from a common alanine precursor. This approach reduces the synthetic difficulty for many αAAs by bypassing the requirement for stereocontrol at Cα, and relies on straightforward and convergent single-bond coupling transformations at the β-methyl position of alanine to access a wide range of β-mono-substituted αAAs. Moreover, these β-mono-substituted αAAs can undergo further C−H functionalization at the β-methylene position to generate various β-branched αAAs in a stereoselective and programmable fashion. These new strategies offer readily applicable methods for synthesis of challenging αAAs and facilitate the efficient total synthesis of complex peptide natural products.



## Yoko Saikawa

Associate Professor
Department of Applied Chemistry, Faculty of Science and Technology, Keio University
Address: 3-14-1 Hiyoshi, Kohoku-ku, Yokohama 223-8522, Japan
Tel & Fax: (+81)-45-566-1562
E-mail: saikawa@applc.keio.ac.jp

### ➢ Educational Background

1998 B.Sc., Keio University (supervisor: Prof. Masaya NAKATA)
2000 M.Sc., Graduate School of Science and Technology, Keio University (supervisor: Prof. Masaya NAKATA)
2004 Doctor of Science, Graduate School of Science and Technology, Keio University (supervisor: Prof. Masaya NAKATA)

### ➢ Professional Career

2002 Research Assistant, Keio University
2007 Assistant Professor, Keio University
2008 Visiting Scholar, Harvard Medical School (~2009, with Prof. Jon Clardy)
2014 Associate Professor, Keio University

### ➢ Research Interests

1) Total synthesis of natural products
2) Isolation and structure determination of bioactive natural products

### ➢ Awards

2003 Incentive Award of 45th Symposium on the Chemistry of Natural Products
2014 CSJ Award for Outstanding Young Women Chemists

### ➢ Recent Publications

1. "Synthesis and Biological Evaluation of Kendomycin and Its Analogues" Tanaka, K.; Matsuyama, H.; Watanabe, M.; Fujimori, Y.; Ishibashi, K.; Ozawa, T.; Sato, T.; Saikawa, Y.; Nakata. M. *J. Org. Chem.* **2014**, *79*, 9922–9947.
2. "Smooth Isoindolinone Formation from Isopropyl Carbamates via Bischler-Napieralski-type Cyclizaion" Adachi, S.; Onozuka, M.; Yoshida, Y.; Ide, M.; Saikawa, Y.; Nakata, M. *Org. Lett.* **2014**, *16*, 358–361.
3. "Total Syntheses of Lactonamycin and Lactonamycin Z with Late-Stage A-Ring Formation and Glycosylation" Adachi, S.; Watanabe, K.; Iwata, Y.; Kameda, S.; Miyaoka, Y.; Onozuka, M.; Mitsui, R.; Saikawa, Y.; Nakata, M. *Angew. Chem., Int. Ed.* **2013**, *52*, 2087–2091.
4. "Total Synthesis of Kendomycin Featuring Intramolecular Dötz Benzannulation" Tanaka, K.; Watanabe, M.; Matsuyama, H.; Ishibashi, K.; Saikawa, Y.; Nakata. M. *Org. Lett.* **2010**, *12*, 1700–1703.

# Synthesis and Biological Evaluation of Antibiotic Polyketides

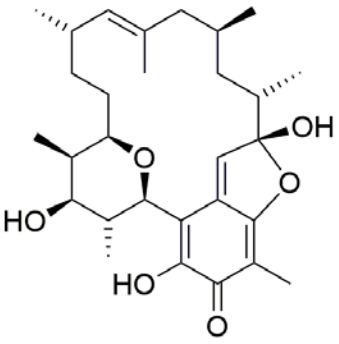
Yoko Saikawa
*Department of Applied Chemistry, Faculty of Science and Technology, Keio University*
*3-14-1 Hiyoshi, Kohoku-ku, Yokohama 223-8522, Japan*

There are a variety of polyketides with complex structure and fascinating bioactivities. We are focusing on the synthesis of such attractive natural products to develop new strategy useful for their syntheses and to reveal the substructure requisite for their bioactivities.

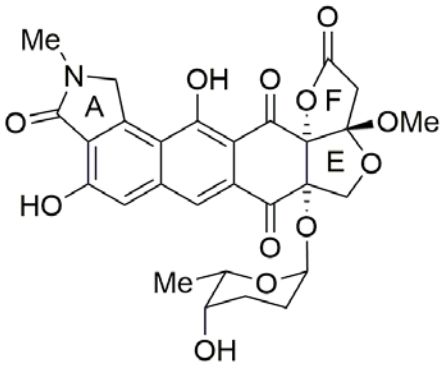
Ansa-type antibiotic kendomycin (**1**) has a unique quinone methide architecture connected to a highly-substituted tetrahydropyran ring and possesses potent antibacterial and cytotoxic activities. **1** was synthesized via intramolecular Dötz reaction which enabled simultaneous aromatization and macrocyclization. Using this efficient method to construct an ansa-skeleton, new ansa-type analogs were also synthesized. Antimicrobial activities of the analogs revealed necessity of the ansa-skeleton.

On the other hand, total synthesis of lactonamycin (**2**), a potent antimicrobial polyketide, was performed via sequential construction of its six rings followed by glycosylation. In the course of the synthesis, we developed a new method for construction of isoindolinone moiety (A-ring), that is modified Bischler-Napieralski reaction. Various model compounds and synthetic intermediates of **2** provided insight into the biological function of its complex structure which is dug down to the individual factors such as γ-lactam (A-ring), EF-ring configuration, and the rhodinose linkage.

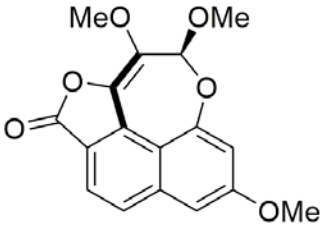
The latest topic of a cytotoxic naphthofuranoxepin dioscorealide A (**3**) consists of its intriguing structural feature and investigation of its asymmetric synthesis via chiral transcription of the synthetic intermediate into **3** with mobile chiral center.



Kendomycin (**1**)

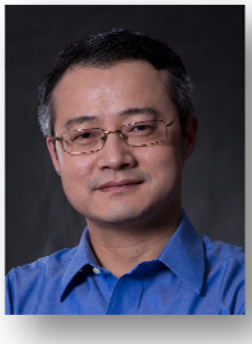


Lactonamycin (**2**)



Dioscorealide A (**3**)

## Wenjun Tang



Research Professor
State Key Laboratory of Bio-Organic & Natural Products Chemistry
Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences
345 Ling Ling Road, Shanghai 200032
Tel: (+0086)-21-54925515
E-mail: tangwenjun@sioc.ac.cn

### ➢ Educational Background

1995 B.Eng., East China University of Sciences and Technology (supervisor: Prof. Guohou Cheng)
1998 M.Sc., Shanghai Institute of Organic Chemistry, CAS (supervisor: Prof. Dawei Ma)
2003 Ph.D., Department of Chemistry, The Pennsylvania State University (supervisor: Prof. Xumu Zhang)

### ➢ Professional Career

2003 Postdoctoral fellow, The Scripps Research Institute (supervisor: Prof. KC Nicolaou)
2005 Senior scientist, Chemical Development, Boehringer Ingelheim Pharmaceuticals Inc.
2009 Principal scientist, Chemical Development, Boehringer Ingelheim Pharmaceuticals Inc.
2011 Research professor, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences

### ➢ Research Interests

1) Design and development of novel, efficient, and practical chiral catalytic reactions;
2) Total synthesis of complex and biologically active natural products;

### ➢ Awards

2012 National “Thousand Talents” Youth program
2012 Thieme Chemistry Journal Award
2015 Asian Core Lectureship Award
2015 National Homogenous Catalysis Youth Award

### ➢ Recent Publications

1. “Transition-Metal-Free Stereospecific Cross-Coupling with Alkenylboronic Acids as Nucleophiles” Li, C.; Zhang, Y.; Sun, Q.; Gu, T.; Peng, H.; Tang, W.* *J. Am. Chem. Soc.* **2016**, 138, 10774.
2. “Synthesis of Chiral 1,4-Benzodioxanes and Chromans by Enantioselective Palladium-Catalyzed Alkene Aryloxyarylation Reactions” Hu, N.; Li, K.; Wang, Z.; Tang, W.* *Angew. Chem., Int. Ed.* **2016,** *55*, 5044
3. “Highly Enantioselective Rhodium-Catalyzed Addition of Arylboroxines to Simple Ketones: Efficient Synthesis of Escitalopram” Huang, L.; Zhu, J.; Jiao, G.; Wang, Z.; Yu, X.; Deng, W.-P.;* Tang, W.* *Angew. Chem., Int. Ed.* **2016**, *55*, 4527.
4. "Synthesis of Chiral α-Amino Tertiary Boronic Esters by Enantioselective hydroboration of α-Arylnamides", A Hu, N.; Zhao, G.; Zhang, Y.; Liu, X.; Li, G.; Tang, W*.. *J. Am. Chem. Soc.* **2015,** *137*, 6746.
5. “Enantioselective Palladium-Catalyzed Dearomative Cyclization for Efficient Synthesis of Terpenes and Steroids” Du, K.; Guo, P.; Chen, Y.; Cao, Z.; Wang, Z,; Tang, W* *Angew. Chem., Int. Ed.* **2015**, *54*, 3033.

# Natural Product Synthesis Facilitated by Ligand Design

Wenjun Tang
*State Key Laboratory of Bio-Organic & Natural Products Chemistry, Shanghai Institute of Organic Chemistry, Shanghai 200032, P.R.China*

The asymmetric intramolecular Heck reaction have become one of most successful method for constructing polycyclic skeletons bearing an all-carbon chiral quaternary center in natural product synthesis. Despite its versatile synthetic utilities, the asymmetric Heck cyclization employs an olefinic starting material which often requires multiple synthetic steps to prepare. In addition, the transformation of its olefinic product to a target molecule is sometimes tedious. An attractive alternative is enantioselective intramolecular dearomative cyclization which employs an often more accessible substrate with an aryl moiety and leads to a multicyclic product bearing an all-carbon quaternary center. Because of the closer resemblance of the cyclic product to a variety of chiral natural products, this method offers advantages over the Heck reaction for the synthesis of a number of chiral polycyclic natural products. The key issue is how to achieve satisfactory reactivity, chemoselectivity, and enantioselectivity by employing an effective chiral ligand. Herein we described the ligand design that have enabled an effective dearomative cyclization and the efficient asymmetric synthesis of several biologically important alkaloids and polyketides.

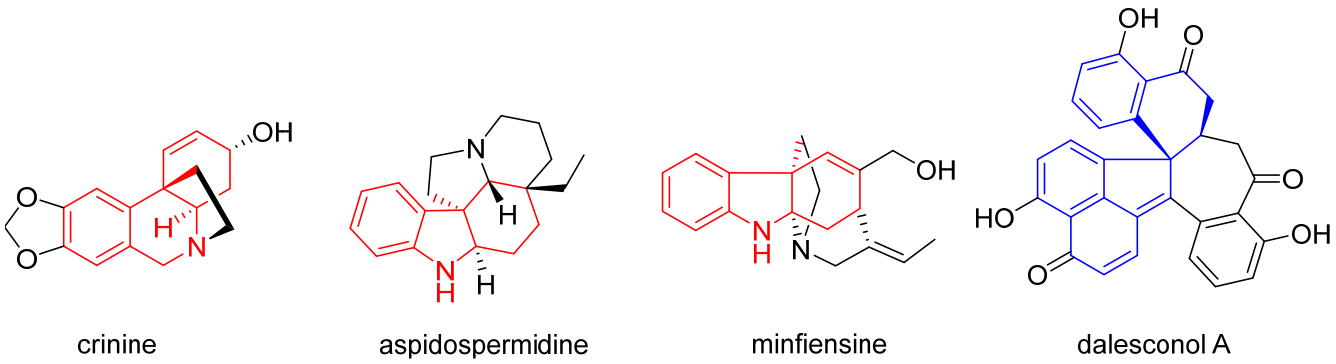



**Figure 1.** Polycyclic natural products

## Go Hirai

Professor
Graduate School of Pharmaceutical Sciences, Kyushu University
Address: 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582, Japan
Tel & Fax: (+81)-92-642-6603
E-mail: gohirai@phar.kyushu-u.ac.jp

### ➢ Educational Background

1997 B.Sc., Tohoku University (supervisor: Prof. Masahiro Hirama)
1999 M.Sc., Graduate School of Science, Tohoku University (supervisor: Prof. Masahiro Hirama)
2002 Doctor of Science, Graduate School of Science, Tohoku University (supervisor: Prof. Masahiro Hirama)

### ➢ Professional Career

2002 Assistant professor, Institute of Multidisciplinary Research for Advanced Materials, Tohoku University (supervisor: Prof. Mikiko Sodeoka)
2004 Research Scientist, Synthetic Organic Chemistry Laboratory, RIKEN (supervisor: Prof. Mikiko Sodeoka)
2010 Senior Research Scientist, Synthetic Organic Chemistry Laboratory, RIKEN (supervisor: Prof. Mikiko Sodeoka)
2016 Professor, Graduate School of Pharmaceutical Sciences, Kyushu University

### ➢ Research Interests

1) Creation of bioactive molecules with unique functions
2) Development of useful molecular tools for understanding glycoconjugates functions

### ➢ Awards

2010 Central Glass Award in Synthetic Organic Chemistry, Japan
2010 Incentive Award in the Pharmaceutical Society of Japan Kanto Branch
2010 Asian Core Program Lectureship Award from Thailand
2014 Incentive Award in Synthetic Organic Chemistry, Japan
2014 Incentive Award 2014 in GlyoTokyo, Japan
2015 Thieme Chemistry Journal Award 2015

### ➢ Recent Publications

1. Photochemical and Additive-Free Coupling Reaction of α-Cumyl α-Keto Esters via Intermolecular C–H Bond Activation, Eisuke Ota, Yu Mikame, Go Hirai, Shigeru Nishiyama, Mikiko Sodeoka. *SYNLETT* **2016,** *26*, 1128-1132.
2. Contribution of Cage-Shaped Structure of Physalins to Their Mode of Action in Inhibition of NF-kB Action, Masaaki Ozawa, Masaki Morita, Go Hirai, Satoru Tamura, Masao Kawai, Ayako Tsuchiya, Kana Oonuma, Keiji Maruoka, and Mikiko Sodeoka. *ACS Med. Chem. Lett.* **2013,** *4*, 730-735.
3. Kinetically Controlled One-Pot Formation of DEFGH-Rings of Type B Physalins through Domino-Type Transformations, Masaki Morita, Go Hirai, Meguni Ohkubo Hiroyuki Koshino, Daisuke Hashizume, Keiji Maruoka, and Mikiko Sodeoka. *Org. Lett.* **2012,** *14*, 3434-3437.

# Synthesis of Monomers for Spectomycin B1, A Middle Size SUMOylation Inhibitor Molecule

Go Hirai,[a,b] Yusaku Nomura,[b] Frederic Thuaud,[b] Daisuke Sekine,[b] and Mikiko Sodeoka[b]
[a]*Graduate School of Pharmaceutical Sciences, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582, Japan*
[b]*RIKEN, 2-1 Hirosawa, Wako, Saitama 351-0198, Japan*

Spectomycin B1 (SMB1) was isolated from *streptomyces spectabilis* in 1994, and its monomeric homolog, spectomycin A1 (SMA1) and A2 (SMA2), were also identified at the same time.[1] Our collaborators Dr. It and Dr. Yoshida recently reported that SMB1 exhibited the inhibitory activity for protein SUMOylation, through direct binding to SUMO-conjugating enzyme E2.[2]

Protein SUMOylation is one of the post-translational modification, in which lysine residue on substrate protein is modified by small ubiquitin-like modifier (SUMO). Dysregulation of SUMOylation pathway is involved in several diseases, and upregulation of enzymes related to SUMOylation was observed in several cancers. Thus, SUMOylation inhibitors would be useful as tools to understand the precise role of SUMOylation as well as candidates for therapeutic agents.

Although the dimeric structure was shown to be requisite for its anti-microbial activity,[1] the effect of SMAs for protein SUMOylation has not been clarified yet due to the unavailability of materials. Furthermore, relative and absolute stereochemistry of SMAs and SMB1 remains to be determined. This time, we synthesized all possible stereoisomers of SMA1 and SMA2, in order to confirm their absolute structures as well as the importance of dimeric structure of SMB1 on inhibitory activity for protein SUMOylation.

We would like to thank Ms. Satoko Maeda, Dr. Akihiro Ito, and Prof. Minoru Yoshida for conducting biochemical experiments. We also thank Dr. Hiroyuki Koshino for NMR measurement, Dr. Daisuke Hashizume for X-ray crystallographic analysis, and Mr. Thomas Cruchter for his kind support.

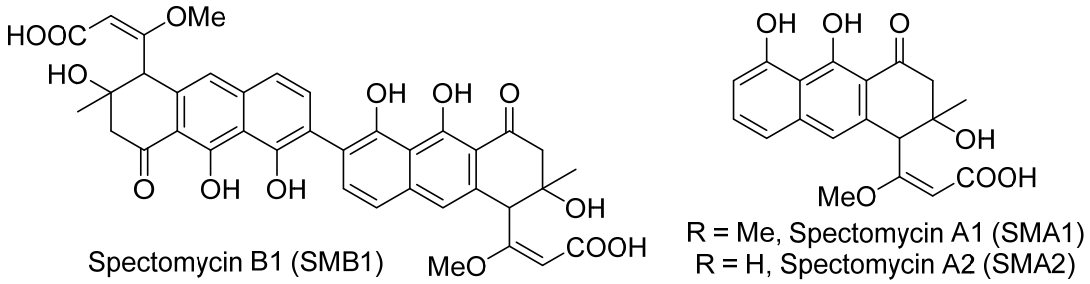



**Figure 1.** Structures of SMB1, SMA1, and SMA2

## References

1. Staley, A. L.; Rinehart, K. L. *J. Antibiot.* **1994**, *47*, 1425-1433.
2. Hirohama, M.; Kumar, A.; Fukuda, I.; Matsuoka, S.; Igarashi, Y.; Saitoh, H.; Takagi, M.; Shin-ya, K.; Honda, K.; Kondoh, Y.; Saito, T.; Nakao, Y.; Osada, H.; Zhang, K. Y.; Yoshida, M.; Ito, A. *ACS Chem. Biol.* **2013**, *8*, 2635-2642.

## Qian Wan

Professor of Chemistry
School of Pharmacy, Huazhong University of Science and Technology
Address: Hangkong Road 13, Wuhan, Hubei, China
Tel & Fax: (+86)-13971060097
E-mail: wanqian@hust.edu.cn

### ➢ Educational Background

1997 B.Sc., Central China Normal University
1999 M.Sc., Paris-Sud (XI) University (supervisor: Prof. Claudine Augé)
2004 Ph.D., Paris-Sud (XI) University (supervisor: Prof. André Lubineau)

### ➢ Professional Career

2004 Research Fellow, Memorial Sloan-Kettering Cancer Center, New York, NY, USA (Advisor: Prof. Samuel J. Danishefsky)
2007 Scientist, Department of Medicinal Chemistry, Amgen Inc., Cambridge, MA, USA
2012 Professor, School of Pharmacy, Huazhong University of Science and Technology
2014 Vice Dean of School of Pharmacy

### ➢ Research Interests

1) Carbohydrate Chemistry
2) Free Radical Chemistry

### ➢ Awards

2017 Asian Core Program Lectureship Award (to Taiwan)
2017 Asian Core Program Lectureship Award (to Singapore)
2015 7th Asian Community of Glycoscience and Glycotechnology Conference Best Poster Award, Miyagi, Japan
2012 "Thousand Talents Program" Young Investigator Award
2011 Amgen First Green Chemistry in Medicinal Chemistry Award

### ➢ Recent Publications

1. "Remote Activation of Disarmed Thioglycosides in Latent-Active Glycosylation *via* Interrupted Pummerer Reaction", Xiao, X.; Zhao, Y.; Shu, P.; Zhao, X.; Liu, Y.; Sun, J.; Zhang, Q.; Zeng, J.; Wan, Q.* *J. Am. Chem. Soc.* **2016,** *138*, 13402.
2. "Glycosylation via Remote Activation of Anomeric Leaving Groups: Development of 2-(2-Propylsulfinyl)benzyl Glycosides as Novel Glycosyl Donors", *Org. Chem. Front.* **2016**, *3*, 177.
3. "Interrupted Pummerer Reaction in Latent-Active Glycosylation: A Novel Type of Glycosyl Donors with Recyclable and Regenerative Leaving Group", *Angew. Chem. Int. Ed.* **2015**, *54*, 14432.
4. "Selective S-deacetylation Inspired by Native Chemical Ligation: Practical Syntheses of Glycosyl Thiols and Drug Mercapto-analogues", Shu, P.; Zeng, J.; Tao, J.; Zhao, Y.; Yao, G.; Wan, Q.* *Green Chem.* **2015**, *17*, 2545.
5. "Stereoselective Synthesis of α-linked 2-Deoxy Glycosides Enabled by Visible Light Mediated Reductive Deiodination", Wang, H.; Tao, J.; Cai, X.; Chen, W.; Zhao, Y.; Xu, Y.; Yao, W.; Zeng, J.; Wan, Q.* *Chem. Eur. J.* **2014**, *20*, 17319.

# Remote Activation of *O/S*-Benzyl Glycosides in Latent-Active Glycosylation

Xiong Xiao, Yueqi Zhao, Yang Xu, Jianchang Sun, Jing Fang, Xiang Zhao, Yan Liu, Lingkui Meng, Jing Zeng and Qian Wan*

*School of Pharmacy, Huazhong University of Science and Technology, Wuhan, Hubei, P. R. China*

Latent *O/S*-glycosides, *O/S*-2-(2-propylthiol)benzyl (PTB) glycosides, were converted into the corresponding active glycosyl donors, *O/S*-2-(2-propylsulfinyl)benzyl (PSB) glycosides, by a simple and efficient oxidation. Treatment of PSB donors and various acceptors with triflic anhydride provided the desired glycosides in good to excellent yields. Three natural hepatoprotective glycosides, Leonuriside B, Leonoside E and F, were synthesized efficiently in a convergent [3+1] manner with this newly developed methods. The total syntheses also led to structural revisions of these phenylethanoid glycosides.

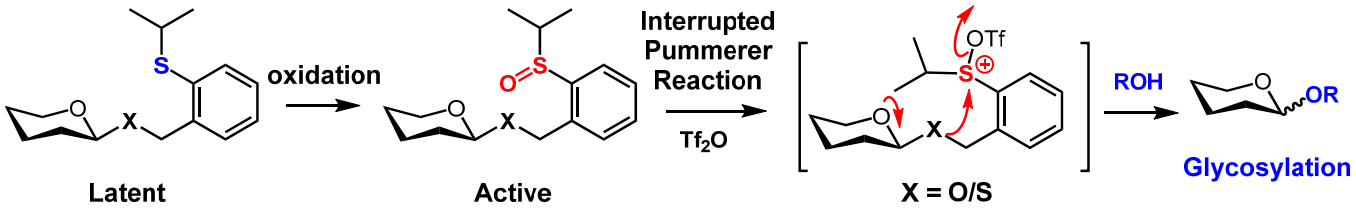
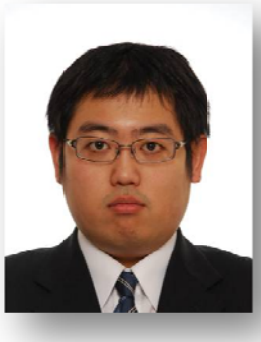



**Figure 1.** Interrupted Pummerer reaction mediated glycosylation

## Yoshiyuki Manabe



Assistant Professor of Chemistry
Department of Chemistry, Graduate School of Science, Osaka University
Address: 1-1 Machikaneyama, Toyonaka, Osaka 560-0043, Japan
Tel & Fax: (+81)-6-6850-5391
E-mail: manabey12@chem.sci.osaka-u.ac.jp

### ➢ Educational Background

2006 B.Sc., Faculty of Science, Tohoku University, (supervisor: Prof. Minoru Ueda)
2008 M.Sc., Graduate School of Science, Tohoku University (supervisor: Prof. Minoru Ueda)
2011 Doctor of Science, Graduate School of Science, Tohoku University (supervisor: Prof. Minoru Ued)

### ➢ Professional Career

2011 Postdoctral fellow, Kyushu University
2012 Assistant professor, Osaka University

### ➢ Research Interests

1) Natural product
2) Glycoscience
3) Chemical biology
4) Organic synthesis

### ➢ Recent Publications

1. "Chemical Synthesis of a Complex-Type *N*-Glycan Containing a Core Fucose.", Nagasaki, M.; Manabe, Y.; Minamoto, N.; Tanaka, K.; Silipo, A.; Molinaro, A. and Fukase, K. *J. Org. Chem.* **2016,** *81*, 10600.
2. "Efficient synthesis of the disialylated tetrasaccharide motif in *N*-glycan via an amide protection strategy.", Zhou, J.; Manabe, Y.; Tanaka, K. and Fukase, K. *Chem. Asian. J.* **2016**, *11*, 1436.
3. "Synthesis of the Conjugates of Tumor Antigens with Adjuvants for the Efficient Cancer Immunotherapy.", Manabe, Y.; Chang, T-C.; Li, H-S.; Terao, N.; Takamatsu, S.; Tanemura, M.; Miyoshi, E. and Fukase, K. *Peptide Science* **2015**, 77.
4. "Revisiting Bromination of C-H Bonds with Molecular Bromine Using a Photo-Microflow System.", Manabe, Y.; Kitawaki, Y.; Nagasaki, M.; Fukase, K. Matsubara, H.: Hino Y.; Fukuyama, T. and Ryu, I. *Chem. Eur. J.* **2014**, *20*, 12750.
5. "Efficient Glycosylation Using $In(OTf)_3$ as a Lewis Acid: Activation of *N*-Phenyltrifluoroacetimidate or Thioglycosides with Halogenated Reagents or PhIO.", Salmasan, R. M.; Manabe, Y.; Kitawaki, Y.; Chang, T.-C.; Fukase, K. *Chem. Lett.* **2014**, *43*, 956.

# Development of the Novel Cancer Immunotherapy Utilizing α-Gal

Yoshiyuki Manabe and Koichi Fukase
*Department of Chemistry, Graduate School of Science, Osaka University, 1-1 Machikaneyama, Toyonaka, Osaka 560-0043, Japan*

α-Gal epitope (Fig. 1) is a trisaccharide produced in most mammals except in humans. On the other hand, humans produce large amount of anti-Gal antibodies which interact specifically with the α-gal epitope. Cancer immunotherapy is a promising therapy that utilizes the patient's own immune system. Although this therapy has the potential to treat the systemic metastatic cancer, its applications are still limited because of the weak antigenicity of tumor antigens. In this study, we developed novel cancer immunotherapy utilizing the hyperacute immune response induced by α-gal epitope.

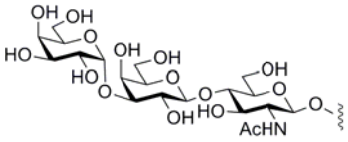
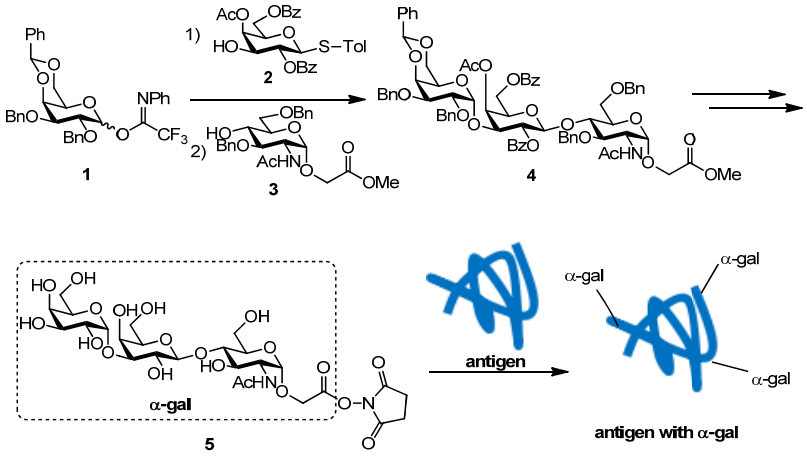


**Fig.1** α-gal epitope

It has already been reported that the expression of α-gal on antigens promotes its uptake owing to the interaction of α-gal and anti-Gal antibody to increase the anti-tumor immunoresponses.[1] We achieved the efficient synthesis of α-gal and conjugation of α-gal with various antigens (Scheme 1). After the one-pot glycosylation of compounds **1**, **2** and **3**, obtained trisaccharide was converted to α-gal succinimidyl ester **5**. Various antigens were then labeled with α-gal using **5**. We also carried out the *in vivo* immunization of α-gal conjugated antigens. As the results, production of antibodies was dramatically increased when we vaccinated with α-gal conjugated antigens in comparison to vaccination without α-gal epitope. We therefor successfully showed that chemically synthesized α-gal can be used as an adjuvant (additive to enhance the immune response to the vaccines) for cancer immunotherapy.[2]




**Scheme 1.** Synthesis of α-gal and conjugation with antigens.

We also investigated cancer immunotherapy using α-gal labeled cancer antibody (Fig. 2). The cancer cells treated with this α-gal labeled antibody were killed by hyperacute rejection.

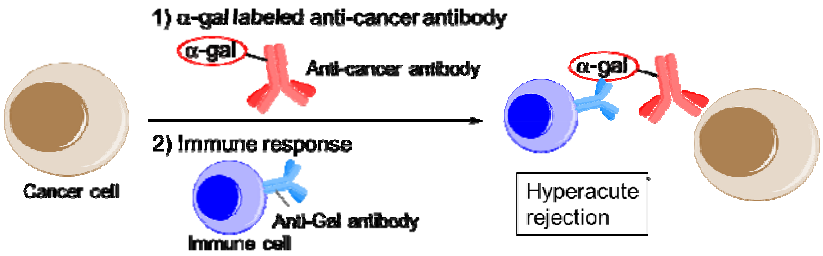



**Fig.2.** α-gal epitope

## Refeences

1. Tanemura, M., Miyoshi, E., Nagano, H., Eguchi, H., Taniyama, K., Kamiike, W., Mori, M., Doki, Y. (2013) *Cancer. Sci.* **104**, 282-290.
2. Japan Patent Application No.2014-263056, Miyoshi, E., Fukase, K., Manabe, Y., Takamatsu, S., Tanemura, M. (2014).

# Chuang-Chuang Li

Research Professor of Chemistry
South University of Science and Technology of China
Address: South University of Science and Technology of China, Shenzhen 518055, China
Tel & Fax: 86-755-8801-8333
E-mail: ccli@sustc.edu.cn

## ➢ Educational Background

2001 B.Sc., China Agricultural University
2006 Ph. D. Peking University (supervisor: Prof. Zhen Yang)
2008 Postdoctoral Fellow, The Scripps Research Institute (supervisor: Prof. Phil S. Baran)

## ➢ Professional Career

2008 Associate professor, Peking University, Shenzhen Graduate School
2014 Research Professor, South University of Science and Technology of China

## ➢ Research Interests

1) Total Synthesis of Natural Products
2) Development of Novel Synthetic Methodology

## ➢ Awards

2016 Leading Talent of Millions of People in Guangdong Province
2015 NSFC Outstanding Young Scholar Award
2014 First-Class Guangdong Natural Science Award
2013 First-Class Shenzhen Natural Science Award

## ➢ Recent Publications

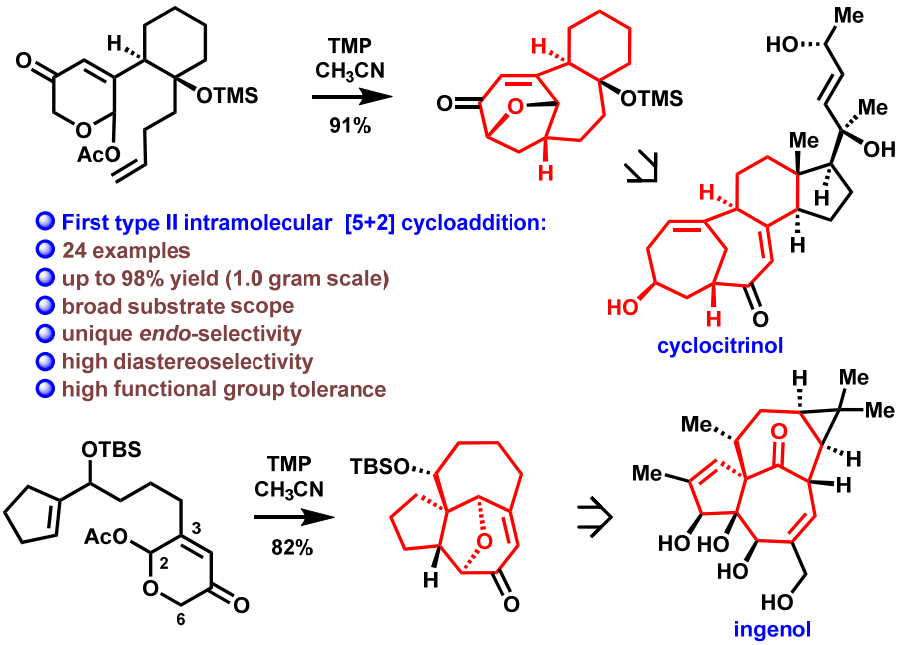
1. Type II Intramolecular [5+2] Cycloaddition: Facile Synthesis of Highly Functionalized Bridged Ring Systems. Mei, G.; Liu, X.; Qiao, C.; Chen, W.; Li, Chuang-Chuang* *Angew. Chem. Int. Ed.*, **2015**, *54*, 1754, doi: 10.1002/anie.201410806.
2. Collective Synthesis of Humulanolides Using a Metathesis Cascade Reaction. Han, J.; Li, F.; Li, Chuang-Chuang* *J. Am. Chem. Soc.*, **2014**, *136*, 13610.
3. Dearomative Indole [5+2] Cycloaddition Reactions: Stereoselective Synthesis of Highly Functionalized Cyclohepta[*b*]indoles. Mei, G.; Yuan, H.; Gu, Y.; Chen, W.; Chung, L.; Li, Chuang-Chuang* *Angew. Chem. Int. Ed.*, **2014**, *53*, 11051.

1. Stereoselective Total Syntheses of (−)-Flueggine A and (+)-Virosaine B. Wei, H.; Qiao, C.; Liu, G.; Yang, Z.*; Li, Chuang-Chuang *Angew. Chem. Int. Ed.*, **2013**, *52*, 620.

# Type II Intramolecular [5+2] Cycloaddition

Chuang-Chuang Li*
*Department of Chemistry, South University of Science and Technology of China, Shenzhen 518055, P. R. China*

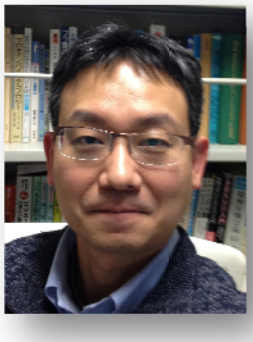
Developing efficient reactions for achieving bridged ring systems is a long-standing challenge but very significant in organic chemistry, considering that such motif is widely found in natural products (such as Taxol®) with significant biological activities. So far there are no general reactions available for the single-step synthesis of bridged seven-membered-ring systems efficiently. Here, we describe the first type II intramolecular [5+2] cycloaddition reaction,[1] which allows the efficient and diastereoselective construction of various highly functionalized and synthetically challenging bridged seven-membered ring systems. This simple, thermal transformation has shown a broad substrate scope and is high yielding, with high functional group tolerance and unique *endo* selectivity. The highly strained tricyclic cores of ingenol mebutate (Picato®) and cyclocitrinol are synthesized efficiently and diastereoselectively using this methodology.




**Reference**

1. (a) Mei, G.; Liu, X.; Qiao, C.; Chen, W.; Li, C.-C. *Angew. Chem. Int. Ed.* **2015**, *54*, 1754. (b) Mei, G.; Yuan, H.; Gu, Y.; Chen, W.; Chung, L.; Li, C.-C. *Angew. Chem. Int. Ed.* **2014**, *53*, 11051.

## Ken Ohmori



Associate Professor of Chemistry
Department of Chemistry, School of Science, Tokyo Institute of Technology
Address: O-okayama, Meguro-ku, Tokyo 152-8551, Japan
Tel & Fax: (+81)-3-5734-2761/2788
E-mail: kohmori@chem.titech.ac.jp

### ➢ Educational Background

1991 B.Sc., Keio University (supervisor: Prof. Shosuke Yamamura)
1993 M.Sc., Department of Chemistry, Keio University (supervisor: Prof. S. Yamamura)
1996 Doctor of Science, Department of Chemistry, Keio University (supervisor: Prof. S. Yamamura)

### ➢ Professional Career

1996 Assistant professor, Tokyo Institute of Technology
2007–present Associate professor, Tokyo Institute of Technology

### ➢ Research Interests

1) Organic Synthesis
2) Natural Product Synthesis
3) Polyphenol Chemistry

### ➢ Awards

1999 Chemical Frontier Award for Young Chemist, 1999
2001 Tejima Memorial Research Award (Nakamura Prize)
2002 Japan Chemical Society Award for Young Chemists
2005 Sankyo Kagaku Award in Synthetic Organic Chemistry
2008 Tokyo Tech Award for Challenging Research
2008 Merck–Banyu Lectureship Award
2011 Tejima Memorial Research Award
2013 Asian Core Program Lectureship Award
2016 SSOCJ Daiichi-Sankyo Award for Medicinal Organic Chemistry

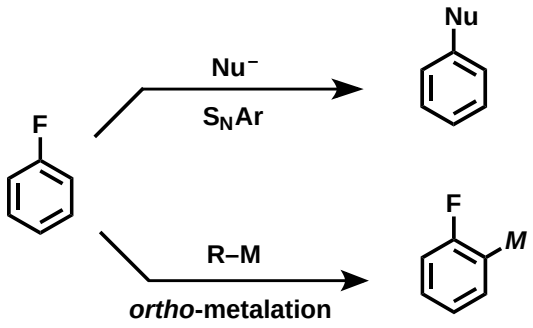
### ➢ Recent Publications

1. "Synthesis and Determination of the Absolute Configuration of Cavicularin by a Symmetrization/ Asymmetrization Approach", H. Takiguchi, K. Ohmori, K. Suzuki, *Angew*. *Chem*. *Int*. *Ed*. **2013**, *52*, 10472–10476.
2. "Annulation Approach to Doubly Linked (A-type) Oligocatechins: Synthesis of (+)-Procyanidin $A_2$ and (+)-Cinnamtannin $B_1$", Y. Ito, K. Ohmori, K. Suzuki, *Angew*. *Chem*. *Int*. *Ed*. **2014**, *53*, 10129–10133.
3. "Flavan–Isoflavan Rearrangement: Bioinspired Synthetic Access to Isoflavonoids via 1,2-Shift–Alkylation Sequence", K. Nakamura, K. Ohmori, K. Suzuki, *Chem*. *Commun*. **2015**, *51*, 7012–7014.
4. "Total Syntheses of Perenniporides, M. Morita, K. Ohmori, K. Suzuki, *Org*. *Lett*. **2015**, *17*, 5634–5637.
5. "Total Synthesis of (+)-Vicenin-2", T.-C. Ho, K. Ohmori, K. Suzuki, *Org*. *Lett*. **2016**, *18*, 4488–4490.
6. "Stereocontrolled Total Syntheses of (–)-Rotenone and (–)-Dalpanol by 1,2-Rearrangement and $S_NAr$ Oxycyclizations", K. Nakamura, K. Ohmori, K. Suzuki, *Angew*. *Chem*. *Int*. *Ed*. **2017**, *56*, 182–187.

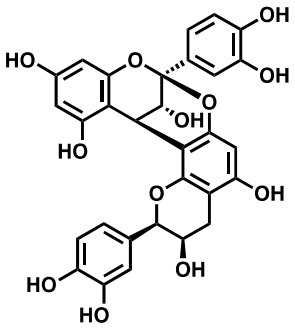
# Aryl Fluorides, a Versatile Synthetic Platform for Natural Product Synthesis

Ken Ohmori
*Department of Chemistry, School of Science, Tokyo Institute of Technology*
*O-okayama, Meguroku, Tokyo 152-8551, Japan*

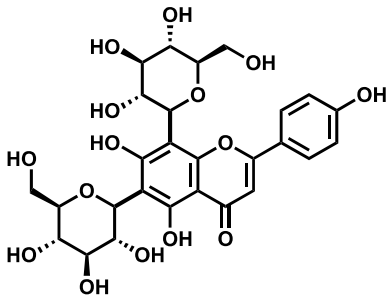
Organofluorine compounds often show unusual chemical properties and behavior in organic reactions. Among them, fluoroaromatic compounds（aryl fluorides) serve great potential as versatile building blocks for synthesis of complex molecules. In this symposium, the author will present some utilities of aryl fluorides in natural product synthesis, where $S_NAr$ reaction and *ortho*-metalation/alkylation sequences are subjected as a key transformation. Details will be discussed in this presentation.



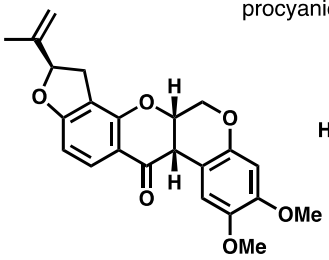

---



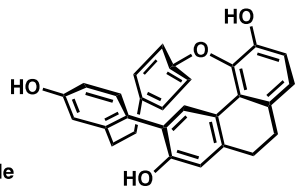

procyanidin A2



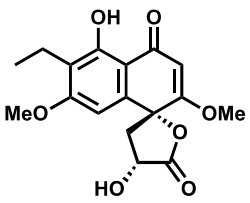

vicenin-2




rotenone

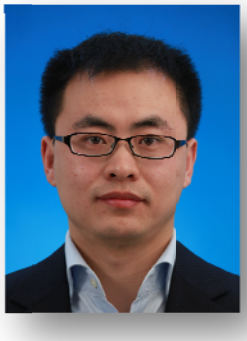



cavicularin




perenniporide A

## Shuanhu Gao



Professor of Chemistry
Shanghai Key Laboratory of Green Chemistry and Chemical Processes
School of Chemistry and Molecular Engineering
East China Normal University
3663N Zhongshan Road, Shanghai 200062, P. R. China
Tel & Fax: (+86)-21-62604784
E-mail: shgao@chem.ecnu.edu.cn

### ➢ Educational Background

2001 B.Sc., Lanzhou University (supervisor: Prof. Yongqiang Tu)
2006 Doctor of Philosophy, Lanzhou University (supervisor: Prof. Yongqiang Tu)

### ➢ Professional Career

2006-2010 Post-doctoral fellow, UT Southwestern Medical Center at Dallas
2010-now Professor at East China Normal University

### ➢ Research Interests

1) Natural products total synthesis
2) Medical chemistry

### ➢ Awards

2016 ACP-Lecture Awards (to Hong Kong and Japan)
2014 NSFC Outstanding Young Scholar Award
2014 Young Investigator Award by Chinese Chemical Society
2014 Thieme Chemistry Journal Award,
2013 New Century Excellent Talents in University Award

### ➢ Recent Publications

1. Total Synthesis of Camptothecin and Related Natural Products by a Flexible Strategy, K. Li, J. Ou, Shuanhu Gao, *Angew. Chem. Int. Ed.* **2016**, *55*, 14778–14783.
2. Total Synthesis of Hamigerans, X. Li, D. Xue, C. Wang, Shuanhu Gao, *Angew. Chem. Int. Ed.* **2016**, *55*, 9942–9946.
3. Total Synthesis of Gracilamine, Yingbo Shi, Baochao Yang, Shujun Cai, and Shuanhu Gao *Angew. Chem. Int. Ed.* **2014**, *53*, 9539-9543.
4. Asymmetric Synthesis and Biosynthetic Implications of (+)-Fusarisetin A, Jun Yin, Cheng Wang, Lili Kong, Shujun Cai, Shuanhu Gao *Angew. Chem. Int. Ed.* **2012**, *51*, 7786-7789.
5. Total Synthesis of Cyanthiwigins A, C, G and H, Wang Cheng, Wang Dan and Gao Shuanhu *Org. Lett.* **2013**, *15*, 4402-4405.

# Total Synthesis of Bioactive Natural Products: Efficiency and Diversity

Shuanhu Gao
*Shanghai Key Laboratory of Green Chemistry and Chemical Processes,*
*School of Chemistry and Molecular Engineering, East China Normal University,*
*3663 Zhongshan N Rd, HuaShiDa, Putuo Qu, Shanghai, P. R. China 200062*

The chemical synthesis of structurally interesting and biologically relevant natural products has served as a driving force for developing new methodologies, testing the scope of existing synthetic methods. It also provides the platform for the further identification of their specific biological targets and mechanistic mode of action. Our research interests are devoted to develop synthetic useful methodologies to address natural target molecules that have novel molecular structure, potent biological activity, and the potential for mechanistic studies.

In this presentation, I will introduce our recent progress in the total synthesis of hamigerans, and structurally related natural products. A newly developed photo-induced enolization/Diels–Alder strategy and its synthetic applications in the synthesis of cordiachrome and anthrabenzoxocinone type natural products will also be discussed.

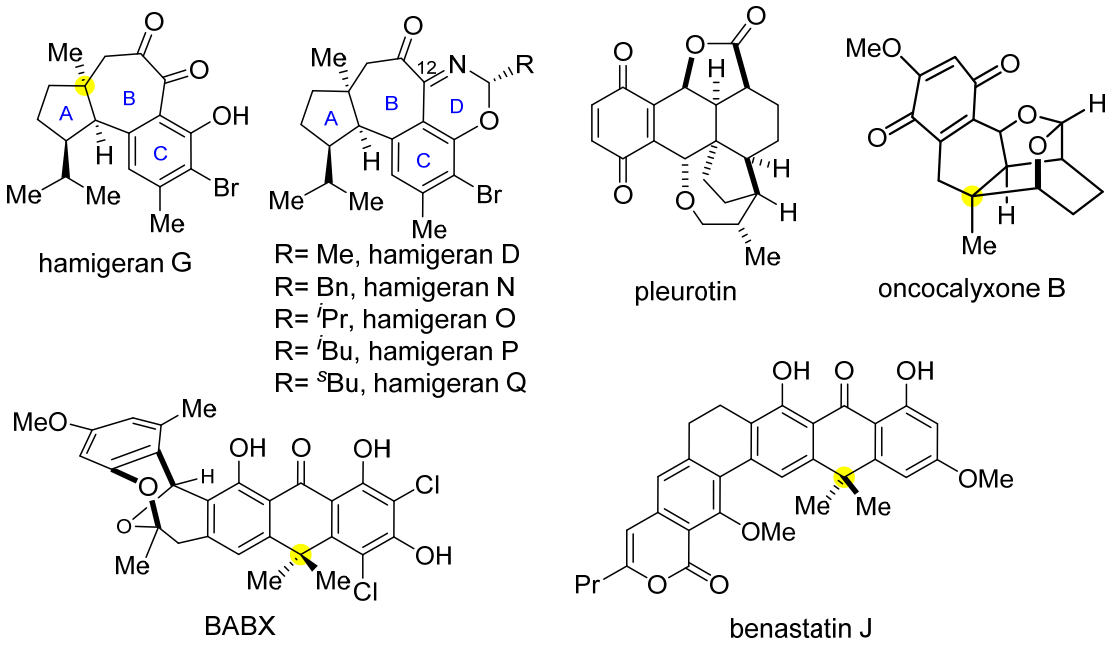



**Figure 1.** Target Molecules

## Hiroki Oguri

Professor of Chemistry
Department of Applied Chemistry, Graduate School of Engineering,
Tokyo University of Agriculture and Technology
Address: 2-24-16 Nakacho, Koganei, Tokyo 184-8588, JAPAN
Tel & Fax: (+81)-42-388-7037
E-mail: h_oguri@cc.tuat.ac.jp

### ➢ Educational Background

1993 B.Sc., Tohoku University (supervisor: Prof. Masahiro Hirama)
1995 M.Sc., Graduate School of Science, Tohoku University (supervisor: Prof. Masahiro Hirama)
1998 Doctor of Science, Department of Chemistry, Graduate School of Science, Tohoku University (supervisor: Prof. Masahiro Hirama)

### ➢ Professional Career

1996 JSPS Research Fellowship for Young Scientist (DC2)
1998 Assistant professor, Tohoku University (Group Head: Prof. Masahiro Hirama)
2003 Visiting Scientist, Harvard University (Group Head: Prof. Stuart L Schreiber)
2004 Associate professor, Hokkaido University (Group Head: Prof. Hideaki Oikawa)
2013 JST-PRESTO Researcher (Molecular Technology, Research Supervisor: Prof. Takashi Kato)
2015 Professor, Tokyo University of Agriculture and Technology

### ➢ Research Interests

1) Design and concise synthesis of skeletally diverse natural products and their analogs
2) Chemical biology with small or mid-sized synthetic molecules
3) Chemo-enzymatic synthesis of natural product analogs

### ➢ Awards

2001 The Inoue Research Award for Young Scientists
2002 The Young Scientist's Research Award in Natural Product Chemistry
2006 The Chemical Society of Japan Award for Young Chemists
2010 Banyu Chemist Award (2010)

### ➢ Recent Publications

1. "Biomimetic assembly lines producing natural product analogs: Strategies from a versatile manifold to skeletally diverse scaffolds" Oguri, H.* *Chem. Rec.* **2016**, *16*, 652.
2. "Synthesis of multiply substituted 1,6-dihydropyridines through Cu(I)-catalyzed 6-*endo* cyclization" Mizoguchi, H.; Watanabe, R.; Minami, S.; Oikawa, H.; Oguri, H.* *Org. Biomol. Chem.* **2015**, *13*, 5955.
3. "Biogenetically inspired synthesis and skeletal diversification of indole alkaloids " Mizoguchi, H.; Oikawa , H.; Oguri, H.* *Nat. Chem.* **2014**, *6*, 57.
4. "Sequential [6+2], [2+2], [3+2] Annulations for Rapid Assembly of Multiple Fragments " Mahendar, V.; Oikawa, H.; Oguri, H.* *Chem. Commun.* **2013**, *49*, 2299.
5. "Generation of anti-trypanosomal agents through concise synthesis and structural diversification of sesquiterpene analogs " Oguri, H.*; Hiruma, T.; Yamagishi, Y.; Oikawa, H.; Ishiyama, A.; Otoguro, K.; Yamada, H.; Ōmura, S. *J. Am. Chem. Soc.* **2011**, *133*, 7096. ***selected as the front cover***.

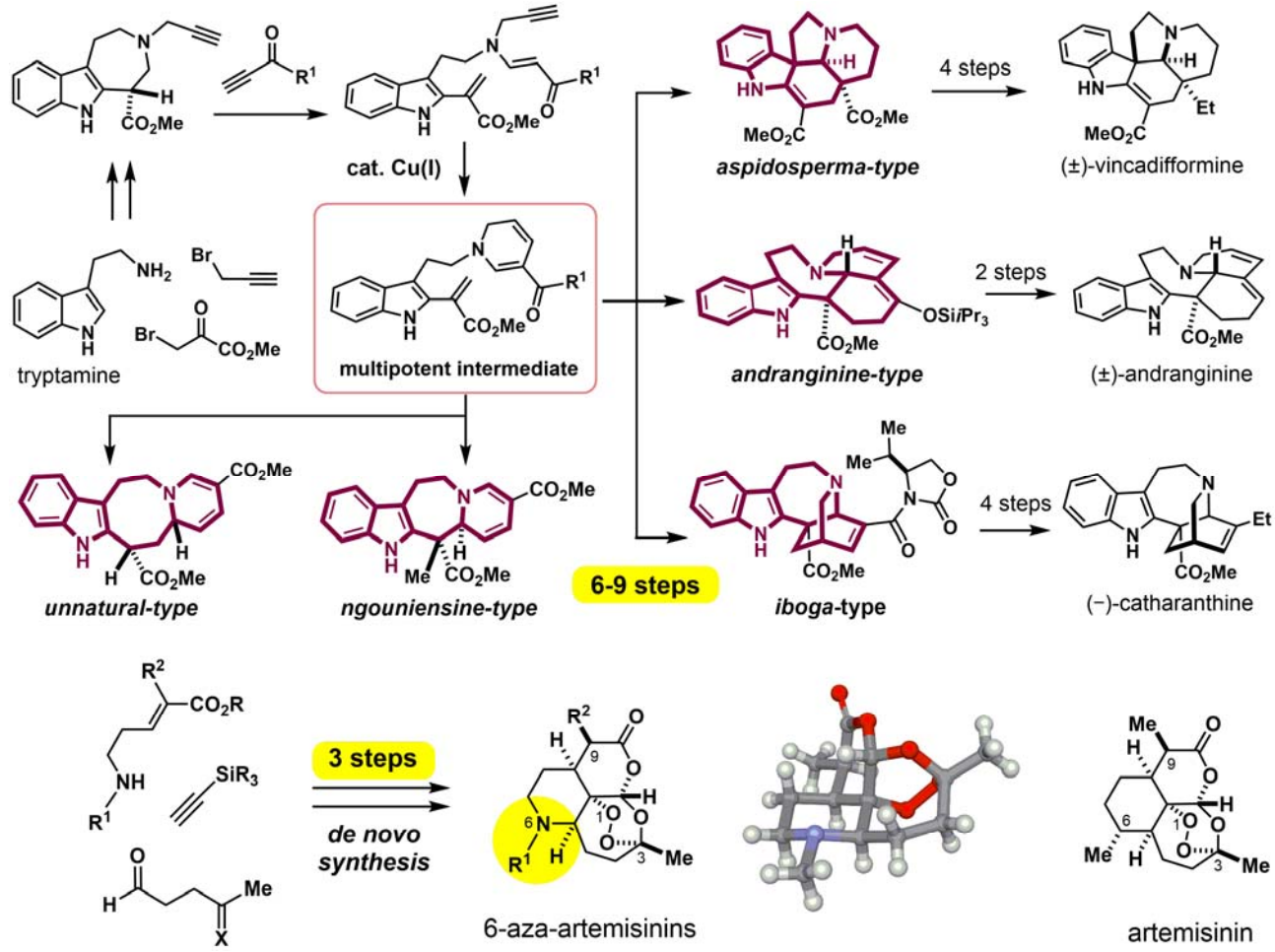
# Development of Chemical Assembly Lines Generating Skeletally Diverse Natural Products and Their Variants

Hiroki Oguri[a,b]

[a]*Department of Applied Chemistry, Graduate School of Engineering,* Tokyo University of Agriculture and Technology, 2-24-16 Nakacho, Koganei, Tokyo 184-8588, *Japan*

[b]*JST-PRESTO, 4-1-8 Honcho, Kawaguchi, Saitama 332-0012, Japan*

Our research group aims to develop chemical assembly lines that concisely generate natural products and their variants having different skeletal, stereochemical and functional group properties. In this forum, I will introduce two topics: (1) Biogenetically-inspired synthesis and skeletal diversification of indole alkaloids, (2) Design and *de novo* synthesis of anti-malarial 6-aza-artemisinins. These approaches could pave the way to rapid and cost-effective production of skeletally diverse, readily modifiable, and natural product-relevant molecules that have been inaccessible by other means.




## References

1) Oguri, H.* *Chem. Rec.* **2016**, *16*, 652.
2) Mizoguchi, H.; Oikawa , H.; Oguri, H.* *Nat. Chem.* **2014**, *6*, 57.
3) Mizoguchi, H.; Watanabe, R.; Minami, S.; Oikawa, H.; Oguri, H.* *Org. Biomol. Chem.* **2015**, *13*, 5955. 4) Reddy, B. K.; Hiruma, T.; Mizoguchi, H.; Ochiai, K.; Suzuki, S.; Oikawa, H.; Ishiyama, A.; Hokari, R.; Iwatsuki, M.; Otoguro, K.; Ōmura, S.; Oguri, H. *submitted*.

## Xiaoguang Lei

Professor of Chemistry
Department of Chemical Biology, College of Chemistry, Peking University
Address: 202 Chengfu Road, Beijing 100871, China
Tel & Fax: (+86)-10-62760292
E-mail: xglei@pku.edu.cn

### ➢ Educational Background

2001 B.Sc., Peking University (supervisor: Prof. Jianbo Wang)
2006 Ph.D., Department of Chemistry, Boston University (supervisor: Prof. John Porco)

### ➢ Professional Career

2006-2008 Postdoc Fellow, Columbia University (supervisor: Prof. Samuel Danishefsky)
2009-2014 Principal Investigator, National Institute of Biological Sciences (NIBS), Beijing
2014- now Professor, Peking University

### ➢ Research Interests

Natural product total synthesis, Chemical biology, and Medicinal chemistry

### ➢ Awards

2017 Tetrahedron Young Investigator Award in Bioorganic and Medicinal Chemistry
2017 Swiss Chemical Society Distinguished Lectureship Award
2017 The David Ginsburg Memorial Lectureship Award
2016 Asian Core Program Lectureship Award
2015 Chemical Society of Japan Distinguished Lectureship Award
2014 Roche Young Investigator Award
2013 Young Chemical Biologist Award by the International Chemical Biology Society

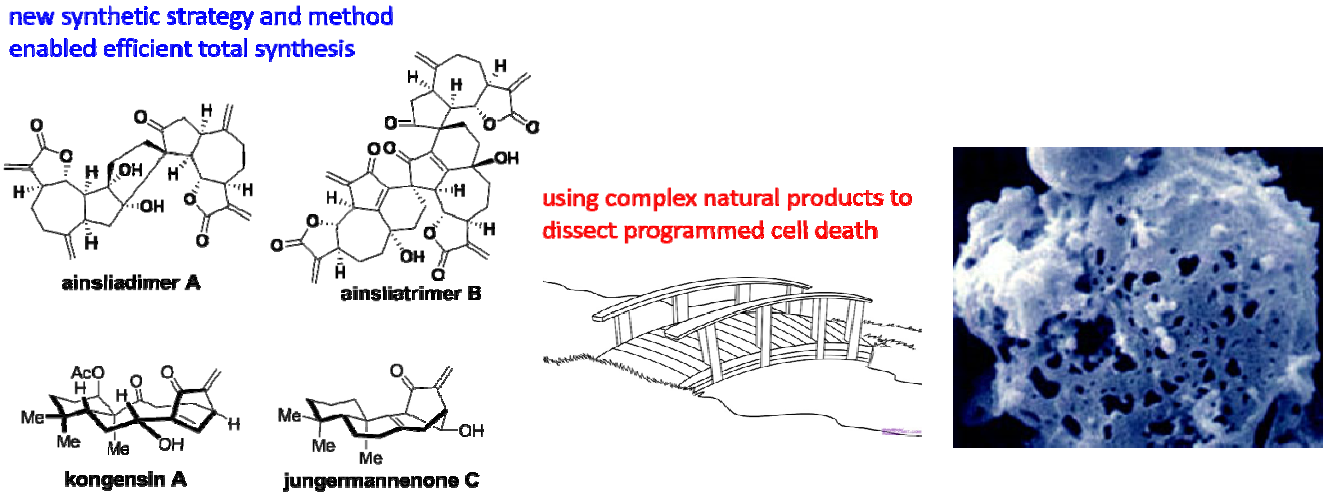
### ➢ Recent Publications

1. Liu, X.; Dong, T.; Zhou, Y.; Huang, N.; **Lei, X.*** "Exploring the Binding Proteins of Glycolipids with Bifunctional Chemical Probes" ***Angew. Chem. Int. Ed.*** **2016**, *55*, 14330-14334.
2. Liu, W.; Li, H.; Cai, P.; Wang, Z.; Yu, Z-X.; **Lei, X.*** "Scalable Total Synthesis of Jungermannenones B and C" ***Angew. Chem. Int. Ed.*** **2016**, *55*, 3112-3116.
3. Hong, B.; Li, C.; Wang, Z.; Chen, J.; Li, H.*; **Lei, X.*** "Enantioselective Total Synthesis of (-)-Incarviatone A" ***J. Am. Chem. Soc.*** **2015**, *137*, 11946-11949.
4. Li, C.; Dong, T.; Li, Q.; **Lei, X.*** "Probing the Anti-cancer Mechanism of (-)-Ainsliatrimer A through Diverted Total Synthesis and Bioorthogonal Ligation" ***Angew. Chem. Int. Ed.*** **2014**, *53*, 12111-12115.
5. Li, Q.; Dong, T.; Liu, X.; **Lei, X.*** "A Bioorthogonal Ligation Enabled by Click Cycloaddition of o-Quinolinone Quinone Methide and Vinyl Thioether" ***J. Am. Chem. Soc.*** **2013**, *135*, 4996-4999.
6. Wang, G.*; Wang, X.; Yu, H.; Wei, S.; Williams, N.; Holmes, D. L.; Halfmann, R.; Naidoo, J.; Wang, L.; Li, L.; Chen, S.; Harran, P.; **Lei, X.***; Wang, X.* "Small Molecule Activation of the TRAIL Receptor DR5 in Human Cancer Cells" ***Nature Chem. Biol.*** **2013**, *9*, 84-89.
7. Sun, L.; Wang, H.; Wang, Z.; He, S.; Chen, S.; Liao, D.; Wang, L.; Yan, J.; Liu, W.; **Lei, X.***; Wang, X.* "Mixed Lineage Kinase Domain-like Protein Mediates Necrosis Signaling Downstream of RIP3 Kinase" ***Cell*** **2012**, *148*, 213-227.
8. Li, C.; Dian, L.; Zhang, W.; **Lei, X.*** "Biomimetic Syntheses of (-)-Gochnatiolides A-C and (-)-Ainsliadimer B" ***J. Am. Chem. Soc.*** **2012**, *134*, 12414-12417.

# Complex Natural Product as a Driving Force for Discovery in Organic Synthesis and Chemical Biology

Xiaoguang Lei
*Department of Chemical Biology, College of Chemistry, Peking University, Beijing 100871, P. R. China*

Complex natural products provide tremendous opportunities to shape the landscape of organic synthesis, as well as to impact the biomedical research and drug discovery. My laboratory conducts research at the interface between chemistry and biology. We systematically use bioactive small molecules, particularly natural products, to study their biological functions, elucidate molecular mechanisms of the important biological pathways, and develop novel therapeutic agents for currently intractable diseases. Herein, I would like to disclose our recent endeavors towards the efficient syntheses of a number of structurally complex and bioactive natural products as well as using the natural product-based chemical probes to dissect programmed cell death.



7th CCS-CSJ Young Chemists Forum 2017

－Frontier in Organic Synthesis toward Middle Molecular Strategy－

■Date　March 18th (Sat), 2017　9:00-17:10

■Venue　S2; Room J24,　House B, Bldg. 4,
Hiyoshi Campus, Keio University
Yokohama, Kanagawa, Japan

■Hosted by
The Chemical Society of Japan (CSJ)
Co-hosted by The Chinese Chemical Society (CCS)

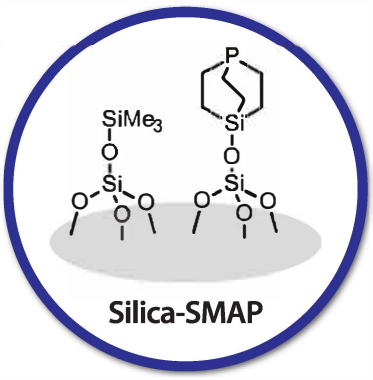
Publication: March 2017
Publisher: The Chemical Society of Japan
1-5, Kanda-Surugadai, Chiyoda-ku Tokyo, 101-8307, Japan

# Silica-SMAP

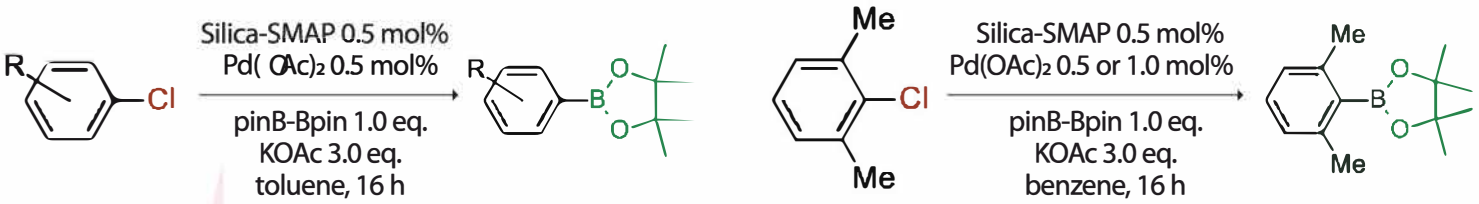
## Cage-type Monophosphine Ligand

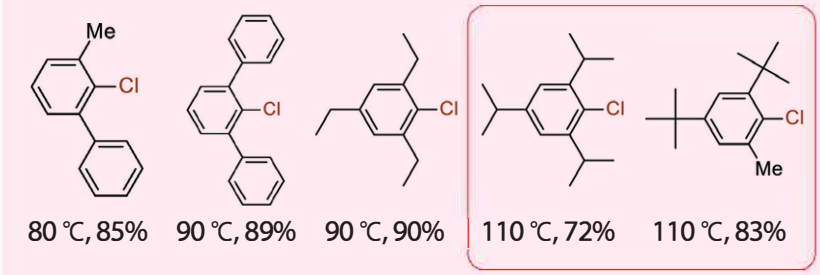
## Features

① Suzuki-Coupling of Ar-Cl substrates
② Borylation of bulky Ar-Cl substrates
③ Regioselective C-H borylation
④ Caged phoshines allow catalysts to be stable in the air.
⑤ Palladium is separated from the products by Celite filtration. [1)]




## Reactions [2),3)]




Borylation of bulky Ar-Cl substrates

| Entry | Ligand | [Pd]/[L] | NMR Yield (%) |
|---|---|---|---|
| 1 | Silica-SMAP | 1:1 | 93 |
| 2 | SPhos | 1:1 | 0 |
| 3 | SPhos | 1:2 | 0 |
| 4 | XPhos | 1:1 | 0 |
| 5 | XPhos | 1:2 | 0 |

Depending Silica-SMAP is a highly on the substrate, active than Buchwald Ligand.

## References


1) Hamasaka, G., Ochida, K., Hara, K., and Sawamura, M. : *Angew. Chem. Int. Ed.*, **46**, 5381 (2007).
2) Kawamorita, S., Ohmiya, H., Iwai, T. and Sawamura, M. : *Angew. Chem. Int. Ed.*, **50**, 8363 (2011).
3) Kawamorita, S., Ohmiya, H.,Hara, K., Fukuoka, A. and Sawamura, M. : *J. Am. Chem. Soc.*, **14**, 5058 (2009).


## Product List

| Product No. | Product Name | Grade | Package size |
|---|---|---|---|
| 197-17451 | Silica-SMAP | Organic Synthesis | 1g |
| 193-17453 | | | 5g |


Wako Pure Chemical Industries, Ltd.

Online Catalog: www.e-reagent.com
USA: labchem@wakousa.com
Europe: biochem@wako-chemicals.de
Others: cservice@wako-chem.co.jp