Hugh Nakamura - C.V. –

Personal

Name Hugh NAKAMURA

Current title Assistant Professor

Department of Chemistry, The Hong Kong University of Science and Technology

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Professional Career

2021–present Assistant Professor (PI), Department of Chemistry, The Hong Kong University of Science and Technology

2017–2021 JSPS Postdoctoral Associate, Scripps Research (La Jolla, California, USA) (Advisor: Professor Phil S. Baran), JSPS Overseas Research Fellowship

Education

2014–2017 Ph.D. Pharmaceutical Sciences, Kyoto University (Kyoto, Japan) (Advisor: Professor Yoshiji Takemoto), JSPS Fellowship DC1

2012–2014 M.S. Pharmaceutical Sciences, Kyoto University (Kyoto, Japan) (Advisor: Professor Yoshiji Takemoto), Japan Student Services Organization Fellowship

2008–2012 B.S. Chemistry, Keio University (Tokyo, Japan) (Advisor: Professor Noritaka Chida)

Research

Postdoc work

Total Synthesis of (–)-Teleocidins and (–)-Taxol (Advisor: Professor Phil S. Baran)

My postdoc work was focused on a unified 11-step total synthesis of natural products of the teleocidin B family. Indolactam V, a known biosynthetic precursor of this family, was accessed by electrochemical amination, copper-mediated ring opening of aziridine, and a remarkable base-induced macrolactamization. To minimize conceding steps, a strategic combination of C-H borylation and Sigman-Heck transformation allowed for a convergent and stereocontrolled synthesis of teleocidins. Taxol, isolated from Taxus brevifolia, possesses miraculous anticancer activity. However, an efficient and scalable strategy has not yet been reported. Hence, we have initiated a project on taxol that can be applied to related natural products. Recently, we have succeeded in the biphasic synthesis of Taxol.

Ph.D. work

Total Synthesis of (–)-Caprazamycin A (Advisor: Professor Yoshiji Takemoto)

My Ph.D. work was focused on the total synthesis of natural products with nitrogen-containing polycyclic structures such as caprazamycin. As a result, I have developed the first total synthesis of caprazamycin A, which has excellent antibacterial properties against Mycobacterium tuberculosis. The highlight of this work is the synthesis of the *syn*-hydroxy-amino acid moiety by a novel bulky thiourea organocatalyzed diastereoselective aldol reaction, which is modular and suitable for future studies in the related natural product.

Honors and Awards

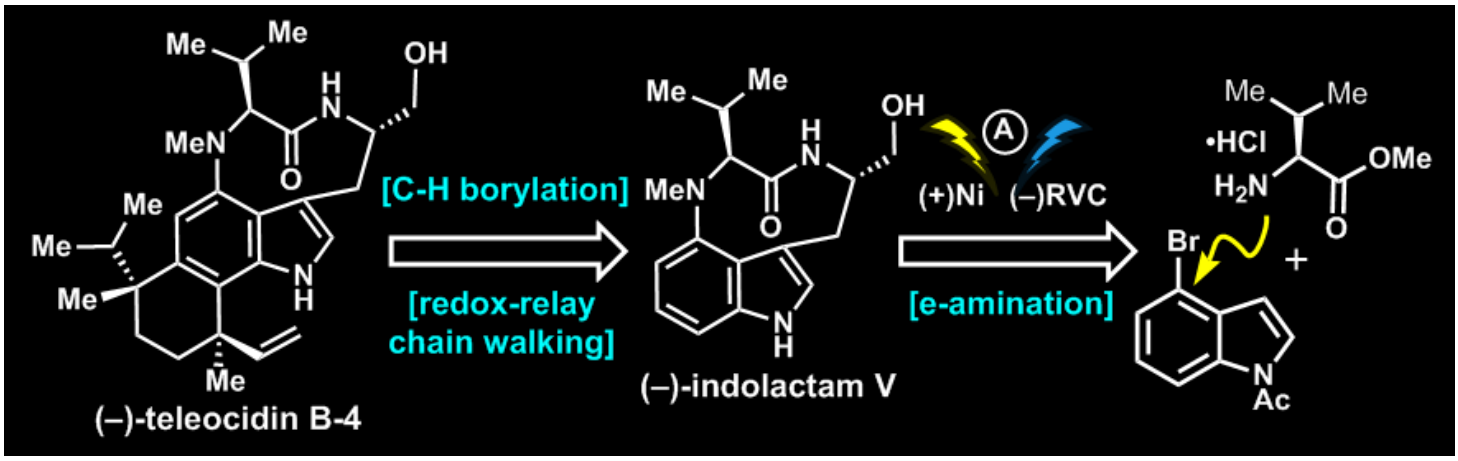
2019	Meeting of Minds@HKU Forum for Outstanding Young Scholars (The University of Hong Kong)
2017–2019	Japan Society for the Promotion of Sciences (JSPS) Postdoctral Fellowship for Research Abroad
2015	The 6th Otsu Academy Award Fellow
2015	The 13th Organic Chemistry the Next Generation Symposium: Best Oral Presentation Award
2014–2017	Japan Society for the Promotion of Sciences (JSPS) Research Fellowship DC1
2014	The 134th Pharmaceutical Society of Japan Annual Convention: Best Oral Presentation Award
2014	The 31st Organic Synthesis Symposium: Best Poster Presentation Award
2012–2014	Japan Student Services Organization Fellowship

Journal Publication

13. **Hugh Nakamura**, Kosuke Yasui, Phil S. Baran

"Total Synthesis of Teleocidins B-1-B-4 by Redox-Relay Chain Walking (RRCW)"

J. Synth. Org. Chem. Jpn. **2021**, *79*, 333−343 DOI: 10.5059/yukigoseikyokaishi.79.333



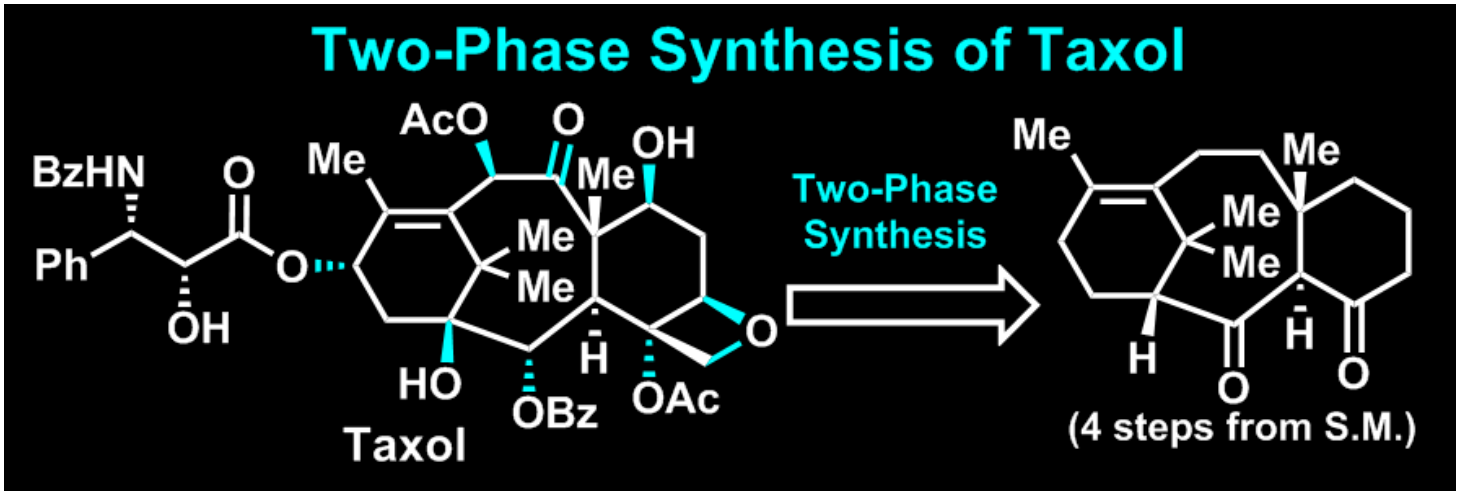
12. Yuzuru Kanda, **Hugh Nakamura**, Shigenobu Umemiya, Ravi Kumar Puthukanoori, Venkata Ramana Murthy Appala, Gopi Krishna Gaddamanugu, Bheema Rao Paraselli, Phil S. Baran

"Two-Phase Synthesis of Taxol"

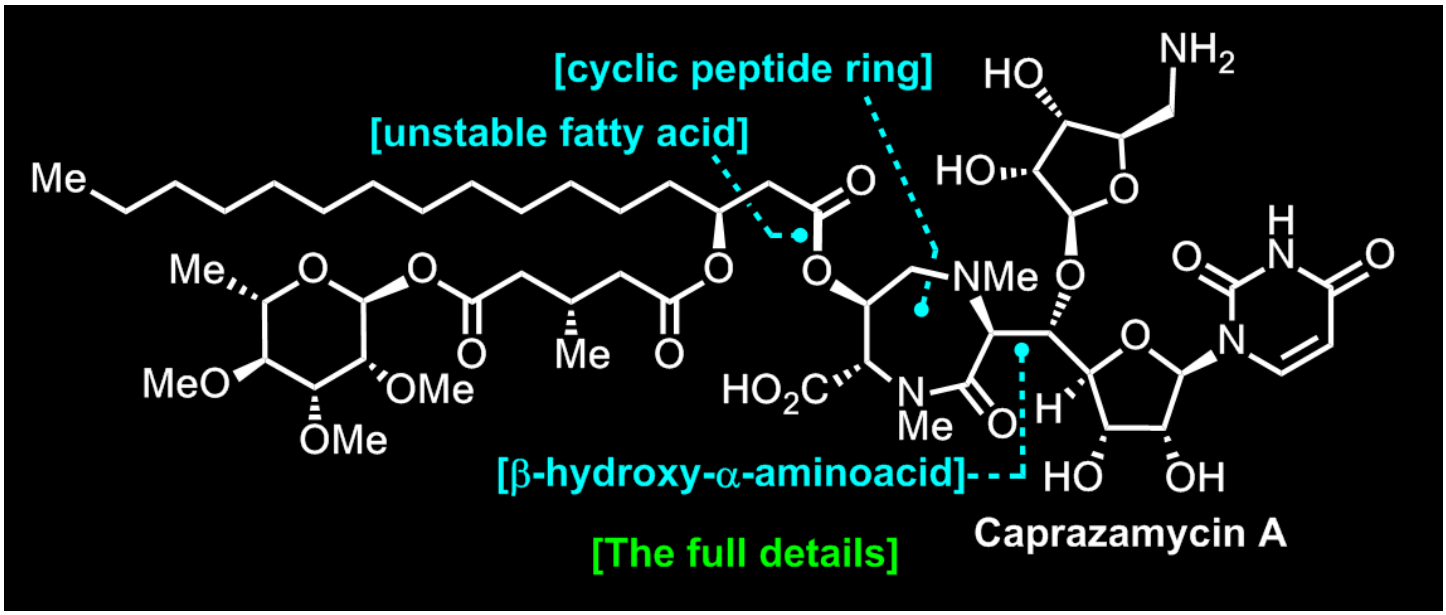
J. Am. Chem. Soc. **2020**, *142*, 10526−10533 DOI: 10.1021/jacs.0c03592

(This article was selected as a Top 20 most downloaded articles in the month)

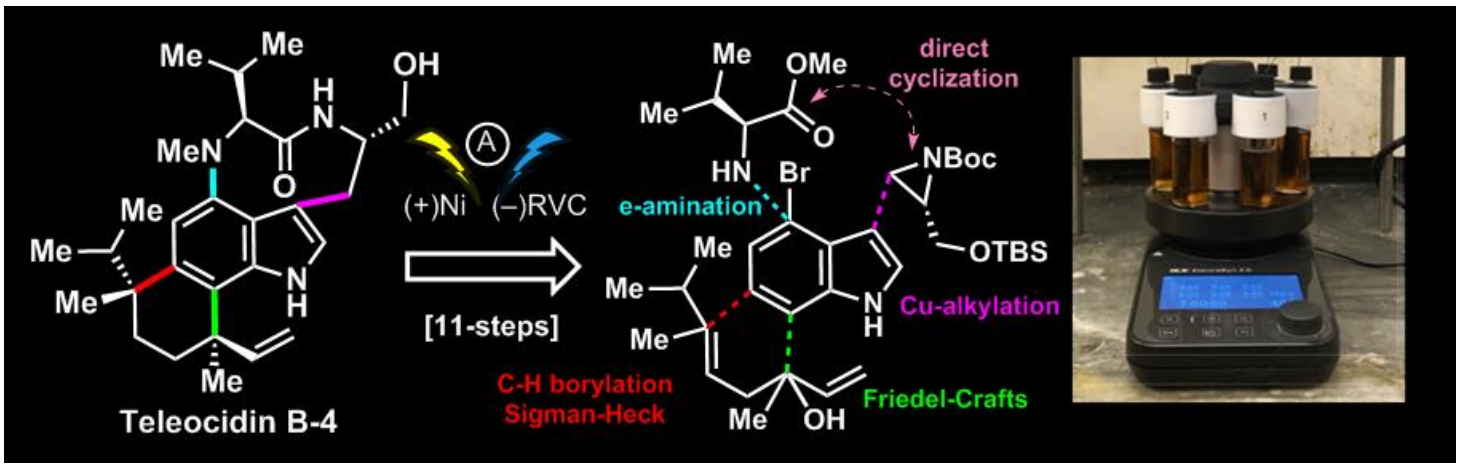
(This article was selected as a Top 20 most downloaded articles in the year)



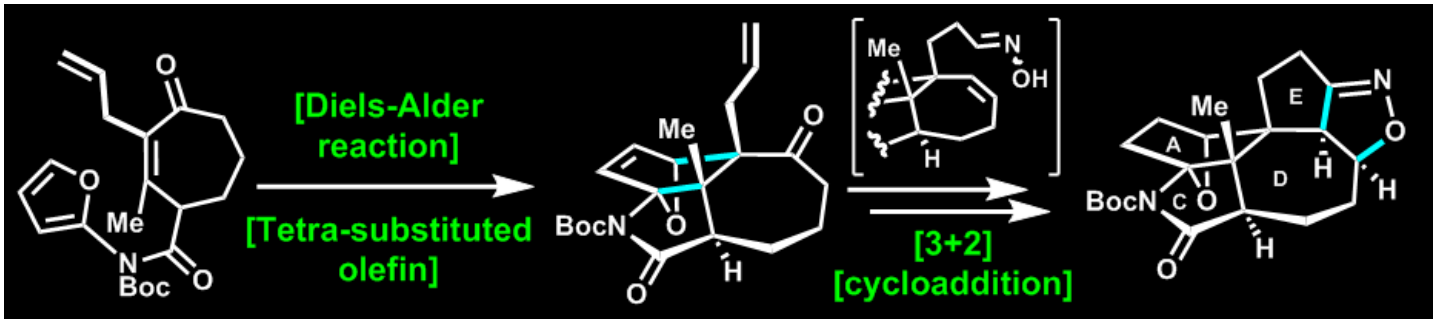
11. **Hugh Nakamura**, Chihiro Tsukano, Takuma Yoshida, Motohiro Yasui, Shinsuke Yokouchi, Yusuke Kobayashi, Masayuki Igarashi, Yoshiji Takemoto
"Total Synthesis of Caprazamycin A: Practical and Scalable Synthesis of syn-β-Hydroxyamino Acids and Introduction of a Fatty Acid Side Chain to 1,4-Diazepanone"
J. Am. Chem. Soc. **2019**, *141*, 8527–8540 **DOI: 10.1021/jacs.9b02220**
(This article was selected as a Top 20 most downloaded articles in the month)



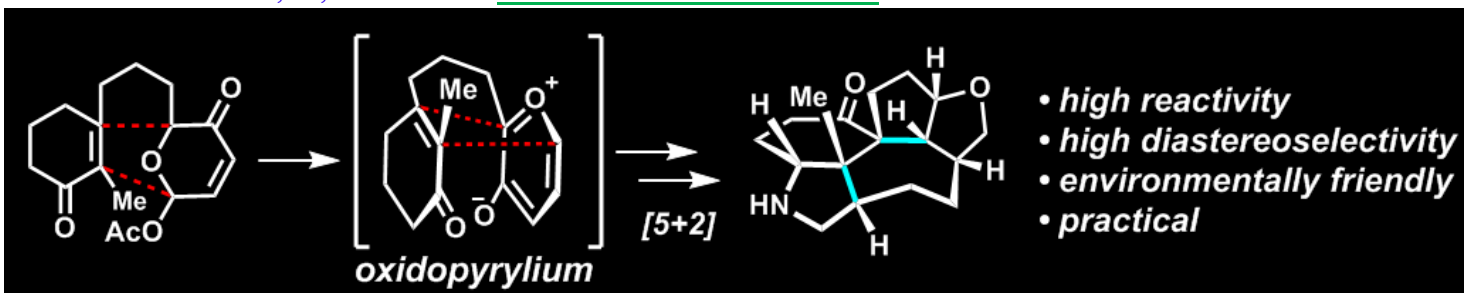
10. **Hugh Nakamura**, Kosuke Yasui, Yuzuru Kanda, Phil S. Baran
"11-Step Total Synthesis of Teleocidins B-1–B-4"
J. Am. Chem. Soc. **2019**, *141*, 1494–1497 **DOI: 10.1021/jacs.8b13697**
(This article was selected as a Top 20 most downloaded articles in the month; Ranked No.1)
(This article was selected as a Top 20 most downloaded articles in the year)
(This article was highlighted in the *Org. Process Res. Dev*. 2019, *23*, 289. **DOI: 10.1021/acs.oprd.9b00092**)



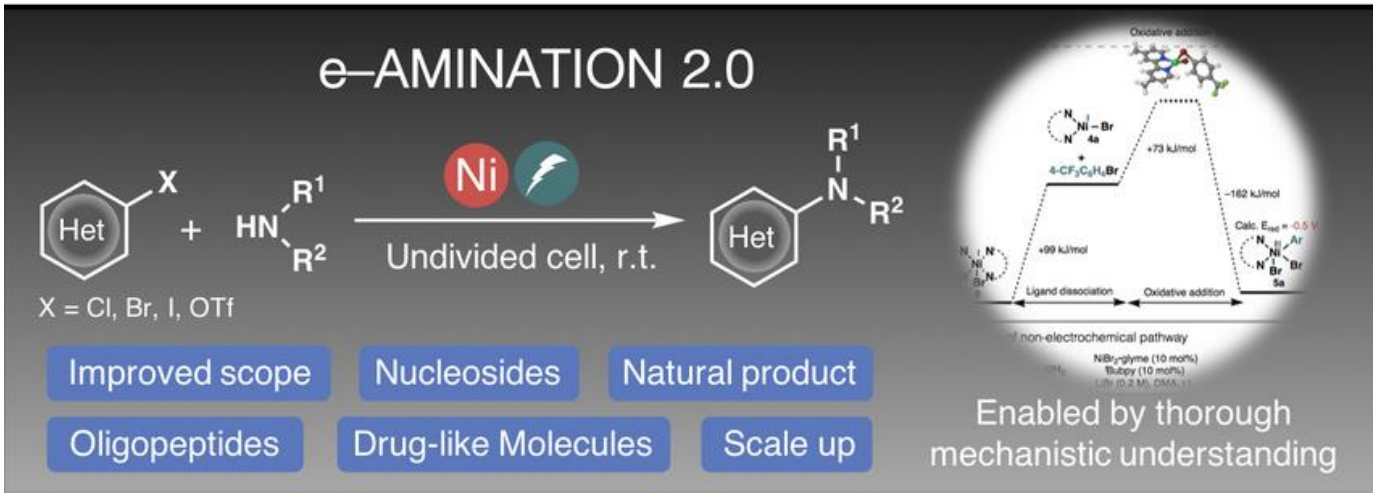
9. **Hugh Nakamura**, Manami Kawakami, Chihiro Tsukano, Yoshiji Takemoto
"Construction of ACDE Ring System of Calyciphylline A-type Alkaloids via Intramolecular Diels-Alder Reaction of a Tetra-substituted Olefin"
Synlett **2019**, *30*, 2253–2257 **DOI: 10.1055/s-0039-1690267**



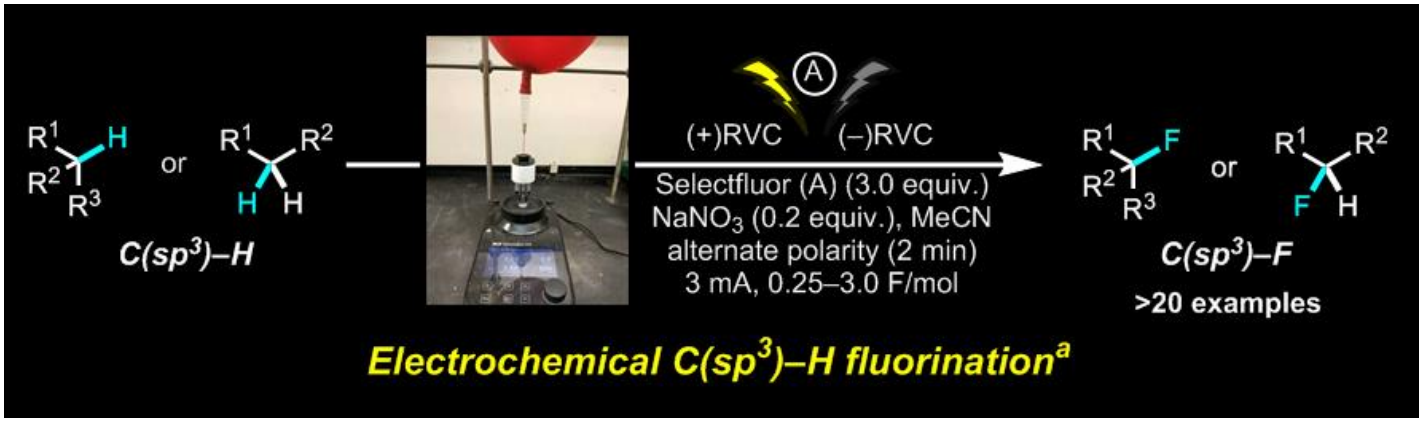
8. **Hugh Nakamura**, Manami Kawakami, Chihiro Tsukano, Yoshiji Takemoto
"Concise construction of the ACDE ring system of calyciphylline A type alkaloids by a [5+2] cycloaddition"
Chem. Eur. J. **2019**, *25*, 8701–8704 **DOI: 10.1002/chem.201901690**



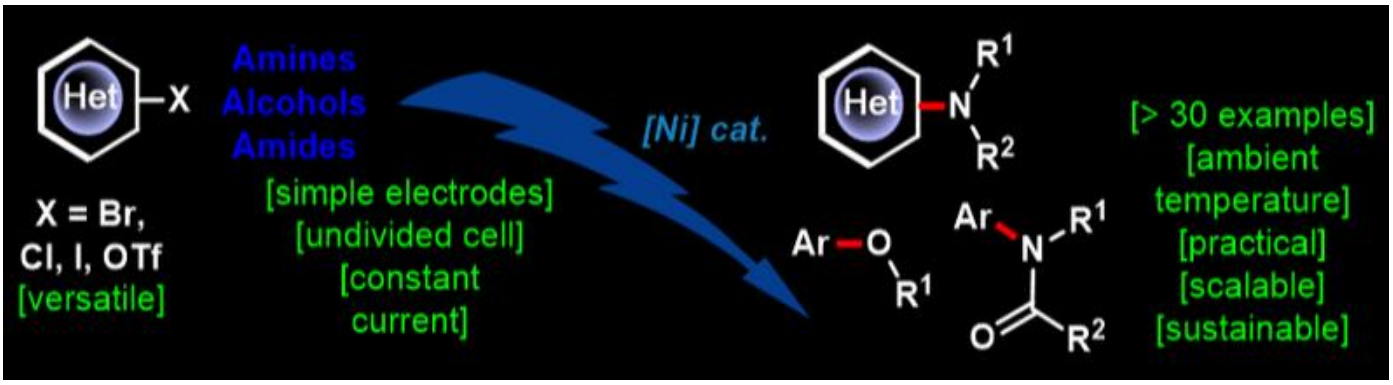
7. Yu K.awamata, Julien C. Vantourout, David P. Hickey, Peng Bai, Longrui Chen, Qinglong Hou, Wenhua Qiao, Koushik Barman, Martin Edwards, Alberto G. Castro, David S. Peters, Justine N. deGruyter, **Hugh Nakamura**, Kyle Knouse, Chuanguang Qin, Khalyd J. Clay, Denghui Bao, Chao Li, Jeremy T. Starr, Neal Sach, Martin D. Eastgate, Matthew Neurock, Shelly D. Minteer, Henry White, Phil S. Baran
"Electrochemically Driven, Ni-Catalyzed Aryl Amination: Scope, Mechanism, and Applications"
J. Am. Chem. Soc. **2019**, *141*, 6392–6402 **DOI: 10.1021/jacs.9b01886**
(This article was selected as a Top 20 most downloaded articles in the month; Ranked No.1)
(This article was selected as a Top 20 most downloaded articles in the year; Ranked No.2)



6. Yusuke Takahira, Miao Chen, Yu Kawamat, Pavel Mykhailiuka, **Hugh Nakamura**, Byron K. Peters, Solomon H. Reisberg, Chao Li, Longrui Chen, Tamaki Hoshikawa, Tomoyuki Shibuguchi, Phil S. Baran
"Electrochemical C(sp³)–H Fluorination"
Synlett **2019**, *30*, 1178–1182 **DOI: 10.1055/s-0037-1611737**
(The 10 most popular articles in the month; Ranked No.1)
(SYNLETT Best Paper Award **2019**) the award received **€ 3000**

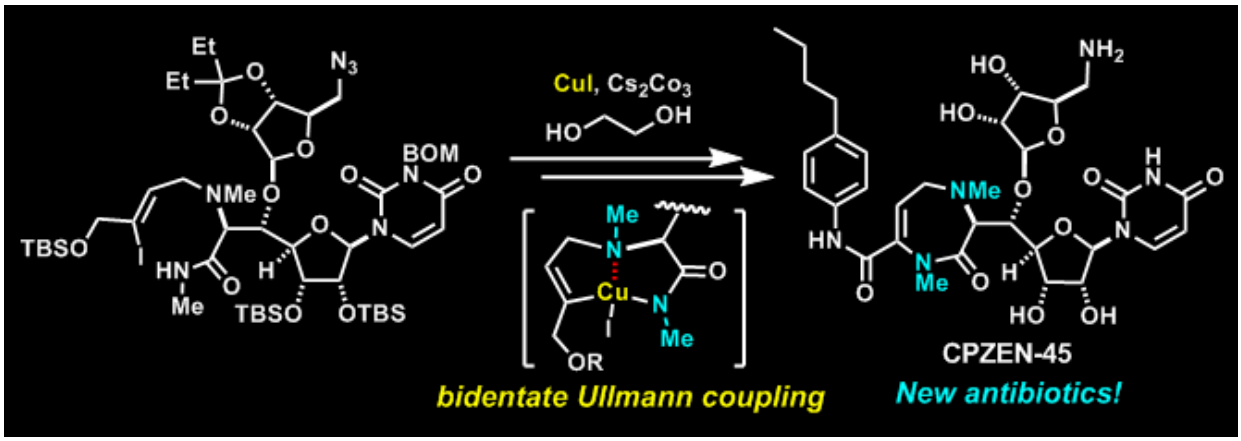


5. Chao Li, Yu Kawamata, **Hugh Nakamura**, Julien C. Vantourout, Zhiqing Liu, Qinglong Hou, Denghui Bao, Jeremy T. Starr, Jinshan Chen, Ming Yan, Phil S. Baran
"Electrochemically Enabled, Nickel-Catalyzed Amination"
Angew. Chem. Int. Ed. **2017**, *56*, 13088–13093 **DOI: 10.1002/anie.201707906**
(This article was selected as a VIP paper.)
(This article was highlighted in the Org. Process Res. Dev. 2017, 21, 1695. **DOI:10.1021/acs.oprd.7b00338**)

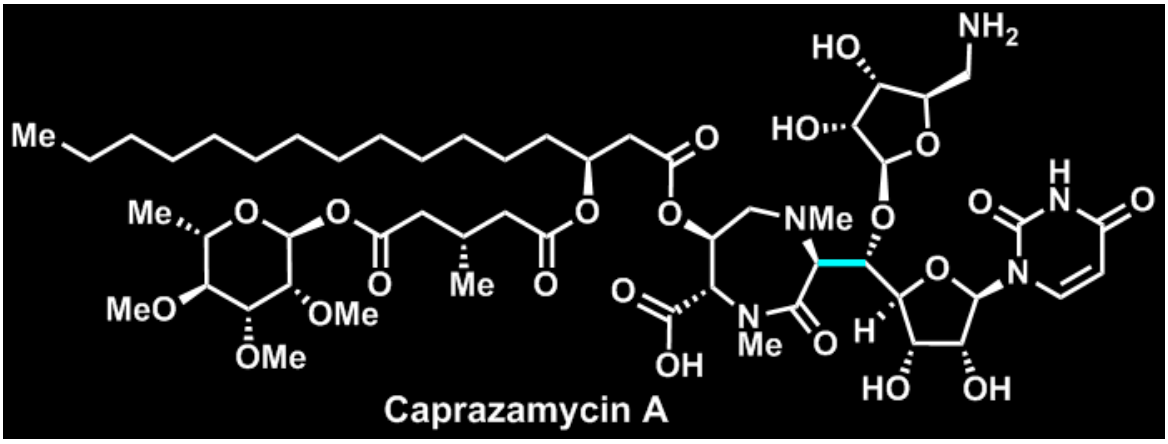


4. **Hugh Nakamura**
"Synthetic studies toward total synthesis of caprazamycins and calyciphylline A type alkaloids"
Dissertation (Ph.D. thesis) **2017**, *Kyoto University* **DOI: 10.14989/doctor.k20298**

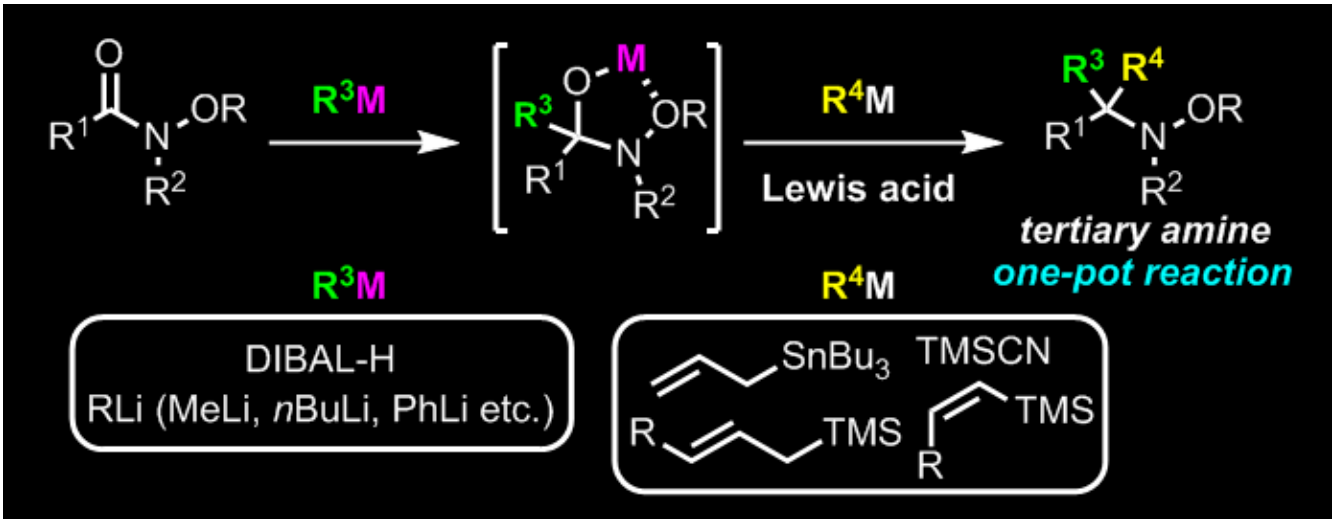
3. **Hugh Nakamura**, Takuma Yoshida, Chihiro Tsukano, Yoshiji Takemoto
"Synthesis of CPZEN-45: Construction of the 1,4-Diazepin-2-one Core by the Cu-catalyzed Intramolecular Amidation of a Vinyl Iodide"
Org. Lett. **2016**, *18*, 2300–2303 **DOI: 10.1021/acs.orglett.6b00943**



2. **Hugh Nakamura**, Chihiro Tsukano, Motohiro Yasui, Shinsuke Yokouchi, Masayuki Igarashi, Yoshiji Takemoto
"Total Synthesis of (−)-Caprazamycin A"
Angew. Chem. Int. Ed. **2015**, *54*, 3136–3139 **DOI: 10.1002/anie.201411954**
(This article was selected as a HOT paper.)



1. Yuta Yanagita, **Hugh Nakamura**, Kenji Shirokane, Yusuke Kurosaki, Takaaki Sato, Noritaka Chida,
"Direct Nucleophilic Addition to *N*-Alkoxyamides"
Chem. Eur. J. **2013**, *19*, 678–684 **DOI: 10.1002/chem.201202639**
（This article was highlighted in Organic Chemistry Portal.）



Major Books and Other Publications

3. **Hugh Nakamura**
"To win away games", Division of Organometallic Chemistry, Kinka Chemical Society, Japan,
Organometallic News, No. 1, 17-18, issued on March 18, 2022

2. **Hugh Nakamura**
"How to survive in the big lab in US", Division of Medicinal Chemistry at The Pharmaceutical Society of Japan,
MEDCHEM NEWS, Vol.31, No. 1, 8-12, 2021

1. **Hugh Nakamura**, Chihiro Tsukano, Yoshiji Takemoto
"Latest Trends in Total Synthesis of Natural Products"
(Area of responsibility: Total Synthesis of Caprazamycin A, a Liponucleoside having Fatty Acids Side Chain)
CMC Publishing CO. LTD. Mar 15, 2020

Invited Talk

1. ○**Hugh Nakamura**
"Total synthesis of highly potent bioactive natural products"
The 4th Organic Chemistry Student Webinar, (Tokyo, Japan, Jan. 2022, Zoom online webinar)

2. ○**Hugh Nakamura**
"The Art and Science of Drug Discovery"
Meeting of Minds@HKU Forum for Outstanding Young Scholars (The University of Hong Kong) (Hong Kong, China, October, 2019)

3. ○**Hugh Nakamura**
"Total Synthesis of Amino acid Containing Natural Products"
Georg-August-University Göttingen (Göttingen, Germany, July, 2019)

Conference Presentations (○Presenter)

4. ○Chihiro Tsukano, **Hugh Nakamura**, Takuma Yoshida, Yoshiji Takemoto
"Synthetic Studies of Sphaerimicin A, a Liponuleoside Antibiotic" (oral presentation)
The 4th International Symposium on Middle Molecular Strategy(ISMMS-4) (Miyagi, Japan, November, 2018)

5. **Hugh Nakamura**, ○Manami Kawakami, Chihiro Tsukano, Yoshiji Takemoto
"Synthetic Studies of Daphniyunnines" (poster presentation)
The 46th Congress of Heterocyclic Chemistry (Kochi, Japan, October, 2017)

6. **Hugh Nakamura**, ○Manami Kawakami, Chihiro Tsukano, Yoshiji Takemoto
"Synthetic Studies of Daphniyunnines" (oral presentation)
The 67th Pharmaceutical Society of Japan in Kinki Annual Convention (Hyogo, Japan, October, 2017)

7. ○Chihiro Tsukano, **Hugh Nakamura**, Takuma Yoshida, Yoshiji Takemoto
"Total Synthesis of Caprazamycin A and CPZEN-45" (invited oral presentation)
Internatinaol Symposium On Pure & Applied Chemistry (ISPCA) 2017 (Ho CHi Minh City, Vietnam, June, 2017)

8. **Hugh Nakamura**, ○Manami Kawakami, Chihiro Tsukano, Yoshiji Takemoto
"Synthetic Studies of Daphniyunnines" (oral presentation)
The 137th Pharmaceutical Society of Japan Annual Convention (Miyagi, Japan, March, 2017)

9. ○**Hugh Nakamura**, Manami Kawakami, Chihiro Tsukano, Yoshiji Takemoto
"Synthetic Studies of Daphnilongeranin B" (oral presentation)
The 42th Symposium on Progress and Synthesis Progress (Shizuoka, Japan, November, 2016)

10. ○Chihiro Tsukano, **Hugh Nakamura**, Takuma Yoshida, Yoshiji Takemoto
"Total Synthesis of CPZEN-45" (oral presentation)
The 110th Organic Synthesis Symposium (Tokyo, Japan, November, 2016)

11. ○Chihiro Tsukano, **Hugh Nakamura**, Takuma Yoshida, Yoshiji Takemoto
"Total Synthesis of Caprazamycin A and CPZEN-45" (poster presentation)
ACP-2016-Korea (Fusion Hall, KI Building KAIST, Daejeon, Korea, October, 2016)

12. Takuma Yoshida, **Hugh Nakamura**, Chihiro Tsukano, ○Yoshiji Takemoto
"Synthesis of CPZEN-45: Construction of the 1,4-Diazepin-2-one Core by Cu-Catalyzed Intramolecular Amidation of a Vinyl Iodide" (poster presentation)
ISHCXX (Kyoto, Japan, July, 2016)

13. **Hugh Nakamura**, ○Manami Kawakami, Chihiro Tsukano, Yoshiji Takemoto
"Construction of 6-7 fused ring bicyclic framework by [5+2] cycloaddition reaction" (poster presentation)
The 136th Pharmaceutical Society of Japan Annual Convention (Kanagawa, Japan, March, 2016)

14. **Hugh Nakamura**, ○Takuma Yoshida, Chihiro Tsukano, Yoshiji Takemoto
"Synthetic Studies of CPZEN-45" (oral presentation)
The 136th Pharmaceutical Society of Japan Annual Convention (Kanagawa, Japan, March, 2016)

15. ○**Hugh Nakamura**, Chihiro Tsukano, Motohiro Yasui, Yoshiji Takemoto
"Total Synthesis of (–)-Caprazamycin A" (oral presentation)
The 9th Seoul-Kyoto-Osaka Joint Symposium (Seoul National University, Korea, November, 2015)

16. ○**Hugh Nakamura**, Chihiro Tsukano, Motohiro Yasui, Yoshiji Takemoto
"Total Synthesis of (–)-Caprazamycin A" (poster presentation)
The 25th ISHC Congress (University of California Santa Barbara, USA, August, 2015)

17. ○**Hugh Nakamura**, Chihiro Tsukano, Motohiro Yasui, Yoshiji Takemoto
"Total Synthesis of (–)-Caprazamycin A" (poster presentation)
The 39th Naito Conference (CHATERAISE Gateaux Kingdom SAPPORO, Japan, July, 2015)

18. **Hugh Nakamura**, ○Takuma Yoshida, Chihiro Tsukano, Yoshiji Takemoto
"Synthetic Studies of CPZEN-45" (poster presentation)
The 45th Congress of Heterocyclic Chemistry (Tokyo, Japan, November, 2015)

19. **Hugh Nakamura**, ○Takuma Yoshida, Chihiro Tsukano, Yoshiji Takemoto
"Synthetic Studies of CPZEN-45" (oral presentation)
The 65th Pharmaceutical Society of Japan in Kinki Annual Convention (Osaka, Japan, October, 2015)

20. ○**Hugh Nakamura**, Chihiro Tsukano, Motohiro Yasui, Yoshiji Takemoto
"Total Synthesis of (–)-Caprazamycin A" (oral presentation)
The 6th Otsu Academy Award Congress (Shiga, Japan, October, 2015)

21. ○**Hugh Nakamura**, Chihiro Tsukano, Motohiro Yasui, Yoshiji Takemoto
"Total Synthesis of (–)-Caprazamycin A" (oral presentation)
The 13th Organic Chemistry the Next Generation Symposium (Shiga, Japan, May, 2015)

22. ○**Hugh Nakamura**, Chihiro Tsukano, Motohiro Yasui, Yoshiji Takemoto
"Total Synthesis of (–)-Caprazamycin A" (oral presentation)
The 135th Pharmaceutical Society of Japan Annual Convention (Hyogo, Japan, March, 2015)

23. **Hugh Nakamura**, ○Takuma Yoshida, Chihiro Tsukano, Motohiro Yasui, Yoshiji Takemoto
"Synthetic Studies of CPZEN-45 : Construction of the 1,4-diazepin-2-one" (oral presentation)
The 135th Pharmaceutical Society of Japan Annual Convention (Hyogo, Japan, March, 2015)

24. ○**Hugh Nakamura**, Chihiro Tsukano, Motohiro Yasui, Yoshiji Takemoto
"Total Synthesis of (–)-Caprazamycin A" (oral presentation)
The 56th Symposium on the Chemistry of Natural Products (Kochi, Japan, October, 2014)

25. **Hugh Nakamura**, ○Takuma Yoshida, Chihiro Tsukano, Yoshiji Takemoto
"Synthetic Studies of CPZEN-45 : Construction of the 1,4-diazepin-2-one by model compound" (oral presentation)
The 64th Pharmaceutical Society of Japan in Kinki Annual Convention (Kyoto, Japan, October, 2014)

26. ○**Hugh Nakamura**, Chihiro Tsukano, Motohiro Yasui, Yoshiji Takemoto
"Synthetic Studies of (–)-Caprazamycin A" (poster presentation)
The 31th Organic Synthetic Chemistry Seminar (Fukuoka, Japan, September, 2014)

27. ○**Hugh Nakamura**, Chihiro Tsukano, Motohiro Yasui, Yoshiji Takemoto
"Synthetic Studies of Caprazamycins" (oral presentation)
The 134th Pharmaceutical Society of Japan Annual Convention (Kumamoto, Japan, March, 2014)

28. Chihiro Tsukano, ○Motohiro Yasui, **Hugh Nakamura**, Kazumi Naoya, Yoshiji Takemoto
"Synthetic Studies of Caprazamycins" (poster presentation)
The 134th Pharmaceutical Society of Japan Annual Convention (Kumamoto, Japan, March, 2014)

29. Chihiro Tsukano, ○**Hugh Nakamura**, Shota Sakamoto, Yoshiji Takemoto
"Synthetic Studies of Caprazamycins" (poster presentation)
The 133th Pharmaceutical Society of Japan Annual Convention (Kanagawa, Japan, March, 2013)

30. Chihiro Tsukano, ○**Hugh Nakamura**, Shota Sakamoto, Shinsuke Yokouchi, Toshifumi Kuribayashi, Yoshiji Takemoto
"Synthetic Studies of Caprazamycins : Construction of the 7-membered diazepanone ring" (oral presentation)
The 62th Pharmaceutical Society of Japan in Kinki Annual Convention (Hyogo, Japan, October, 2012)

31. Chihiro Tsukano, ○**Hugh Nakamura**, Shota Sakamoto, Shinsuke Yokouchi, Toshifumi Kuribayashi, Yoshiji Takemoto
"Synthetic Studies of Caprazamycins" (poster presentation)
The 29th Organic Synthetic Chemistry Seminar (Shizuoka, Japan, September, 2012)

List of third party funded projects

1. 07/2017 – 06/2019 Development of total synthesis of natural product by electrochemistry
Location : Baran group, The Scripps Research Institute, USA
Founded by Japan Society for the Promotion of Science
(114,266 USD)

2. 04/2014 – 03/2017 Total synthesis of caprazamycin A, and development of construction of syn-β-hydroxy amino acid by thiourea organocatalyst
Location : Takemoto group, Kyoto University, Japan
Founded by Japan Society for the Promotion of Science
(93,978 USD)

3. 04/2012 – 03/2014 Synthetic studies of caprazol and caprazamycins
Location : Takemoto group, Kyoto University, Japan
Founded by Japan Student Services Organization
(18,426 USD)

List of teaching experience

06/2019 – now Organic chemistry experimental instruction **(to visiting student from China)**
The Scripps Research Institute, Baran group, USA

01/2019 – 03/2019 Organic chemistry experimental instruction **(to visiting student from Korea)**
The Scripps Research Institute, Baran group, USA

09/2018 – 12/2018	Organic chemistry experimental instruction **(to visiting student from Spain)** The Scripps Research Institute, Baran group, USA
04/2018 – 09/2018	Supervision of the visiting graduate student program **(from Japan)** Topic : Total synthesis of natural product The Scripps Research Institute, Baran group, USA
08/2017 – 02/2018	Organic chemistry experimental instruction **(to graduate student from USA)** The Scripps Research Institute, USA
05/2016 – 06/2016	Supervision of the undergraduate students program Topic : Organic synthesis, purification techniques, NMR, 2D NMR, and IR Kyoto University, Japan
05/2015 – 06/2015	Supervision of the undergraduate students program Topic : Organic synthesis, purification techniques, NMR, 2D NMR, and IR Kyoto University, Japan
05/2014 – 06/2014	Supervision of the undergraduate students program Topic : Organic synthesis, purification techniques, NMR, 2D NMR, and IR Kyoto University, Japan
05/2013 – 06/2013	Supervision of the undergraduate students program Topic : Organic synthesis, purification techniques, NMR, 2D NMR, and IR Kyoto University, Japan
05/2012 – 06/2012	Supervision of the undergraduate students program Topic : Organic synthesis, purification techniques, NMR, 2D NMR, and IR Kyoto University, Japan

Reference

- Prof. Dr. Phil S. Baran (The Scripps Research Institute, USA) email: pbaran@scripps.edu
- Prof. Dr. Yoshiji Takemoto (Kyoto University, Japan) email: takemoto@pharm.kyoto-u.ac.jp
- Prof. Dr. Chihiro Tsukano (Kyoto University, Japan) email: tsukano.chihiro.2w@kyoto-u.ac.jp
- Prof. Dr. Noritaka Chida (Keio University, Japan) email: chida@applc.keio.ac.jp
- Prof. Dr. Takaaki Sato (Keio University, Japan) email: takaakis@applc.keio.ac.jp

Research summary (Ph.D. dissertation)

Research Theme : Total Synthesis of (–)-Caprazamycin A

Affiliation : Kyoto University

Research Outline :

Caprazamycin A (**1**) was isolated from *Streptomyces sp.* by Igarashi and co-workers, which have antibacterial activity against *Mycobacterium tuberculosis* including multidrug-resistant *tuberculosis*. Caprazamycin A (**1**) consists of four fragments, that is, a seven-membered diazepanone core, amino ribose, uridine, and a fatty-acid side chain. The complex structure and significant biological activities of caprazamycins have drawn much attention from synthetic chemists. Matsuda, Ichikawa, and co-workers have accomplished the first total synthesis of caprazol[1], which does not possess a fatty-acid side chain. Last year, Shibasaki, Watanabe, and co-workers also reported the total synthesis of caprazol[2]. However, the total synthesis of the caprazamycins has not yet been reported[3] because of the difficulty in introducing an unstable fatty-acid side chain. Therefore, we initiated a caprazamycin A synthetic project, which would also be applicable to related natural products.

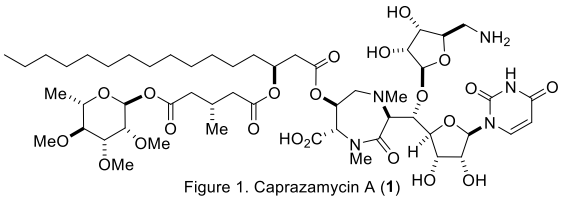
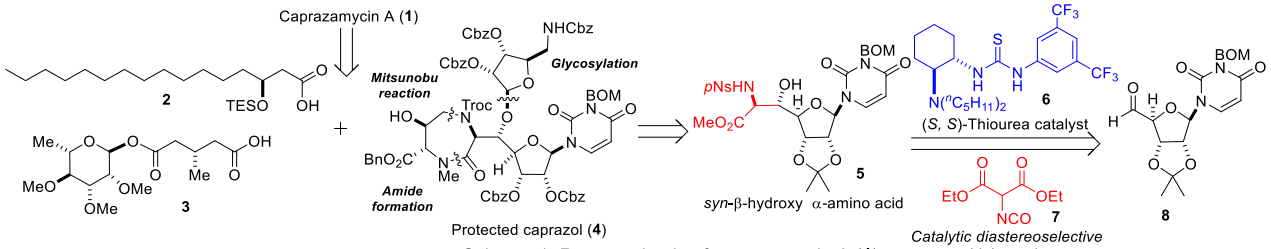


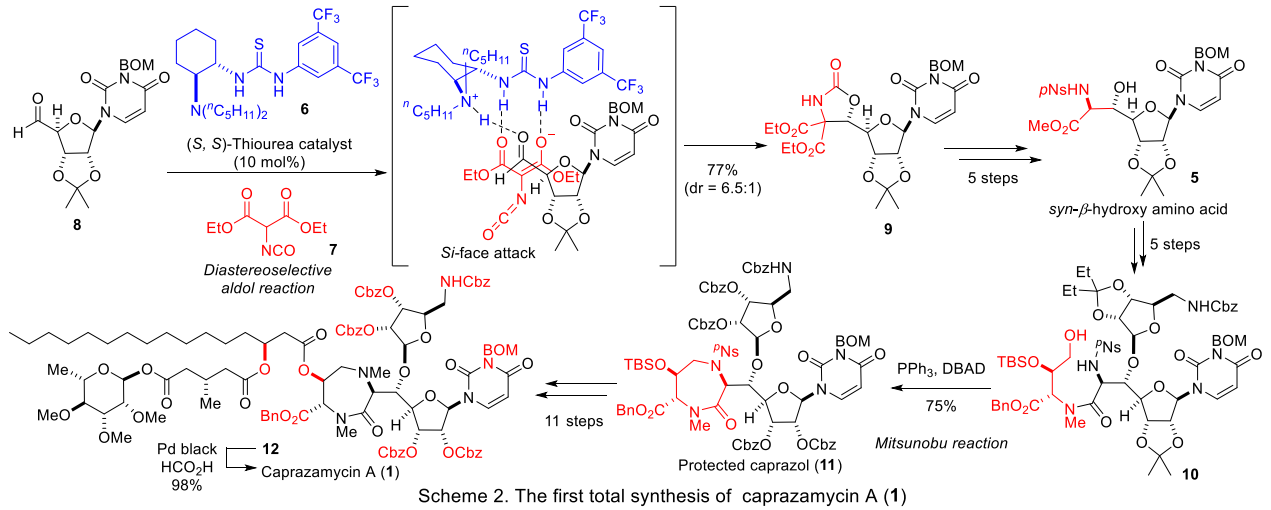
Figure 1. Caprazamycin A (**1**)

Retrosynthesis of caprazamycin A (**1**) is shown in scheme 1. To access caprazamycin A (**1**), it was envisioned that the unstable side chains **2** and **3** could be introduced to the protected caprazol **4** as the final step. This would be followed by global deprotection without adversely affecting any functional groups. The caprazol **4** was prepared using (a) the Mitsunobu reaction to construct the seven-membered diazepanone, and (b) a diastereoselective aldol reaction of the isocyanate **7** and aldehyde **8** with the thiourea catalyst **6** to obtain the *syn*-β-hydroxy α-amino acid derivative **5**.



Scheme 1. Retrosynthesis of caprazamycin A (**1**)

Our synthesis commenced with preparation of *syn*-β-hydroxy α-amino acid derivative **5** with careful control of the stereochemistry at the β-hydroxy α-amino acid moiety (Scheme 2). Diastereoselective aldol reaction of aldehyde **8** with isocyanate **7** and thiourea organocatalyst **6** gave **9** in 77% yield (dr = 6.5:1). The desired compound **9** was converted into *syn*-β-hydroxy α-amino acid derivative **5** in a 5-step procedure. The next challenge was to construct the diazepanone ring system. The Mitsunobu reaction of **10** using PPh_3 and DBAD promoted the seven-membered cyclization without epimerization or other side reactions. The diazepanone core **11** was converted into protected caprazamycin **12** in a 11-step procedure involving stepwise introduction of unstable fatty acid side chains into protected caprazol **11**. Finally, global deprotection with hydrogenation in the presence of palladium black was successful without side-chain decomposition. This step completed the first total synthesis of caprazamycin A (**1**)[4].



Scheme 2. The first total synthesis of caprazamycin A (**1**)

In summary, we have achieved the first total synthesis of caprazamycin A (**1**)[4], which features the following reactions: (a) the scalable preparation of syn-β-hydroxy α-amino acid with a thiourea-catalyzed aldol reaction, (b) construction of a diazepanone with an unstable side chain bearing β-acyloxycarboxylic acid, and (c) global deprotection by single hydrogenation.

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(3) Recently, Shibasaki and co-workers have developed a total synthesis of caprazamycin B; H. Abe, P. Gopinath, G. Ravi, L. Wang, T. Watanabe, M. Shibasaki, *Tetrahedron Lett*. **2015**, *56*, 3782.
(4) H. Nakamura, C. Tsukano, M. Yasui, S. Yokouchi, M. Igarashi, Y. Takemoto, *Angew. Chem. Int. Ed*. **2015**, *54*, 3136.