ウェブサイト公開用

（様式 10）
（海外特別研究員事業）
令和元年 7 月 1 日

海 外 特 別 研 究 員 最 終 報 告 書

独立行政法人 日本学術振興会 理事長 殿

採 用 年 度 平成 29 年
受 付 番 号 311
氏 名 中村 斐有

（氏名は必ず自署すること）

海外特別研究員としての派遣期間を終了しましたので、下記のとおり報告いたします。
なお、下記及び別紙記載の内容については相違ありません。

記

1. 用務地（派遣先国名）用務地：San Diego, California（国名：USA）

2. 研究課題名（和文）※研究課題名は申請時のものと違わないように記載すること。
   酸化的カップリングを利用した herquline 類の超短工程合成

3. 派遣期間：平成 29 年 7 月 1 日 ～ 令和元年 6 月 30 日

4. 受入機関名及び部局名
   Department of Chemistry, The Scripps Research Institute (Baran group)

5. 所期の目的の遂行状況及び成果…書式任意 **書式任意（A4 判相当 3 ページ以上、英語で記入も可）**
（研究・調査実施状況及びその成果の発表・関係学会への参加状況等）
（注）「6. 研究発表」以降については様式 10－別紙 1～4 に記入の上、併せて提出すること。

Postdoctoral Research

My research is focused on simplifying the way molecules are made for the purpose of pharmaceutical, industry, material science and agrochemicals. I have always been obsessed with total chemical synthesis which is such a beautiful one. Because one can be both an artists and an explorer at the same time, so you can paint and you can visit the moon but, you don't have to leave your laboratory to do that.

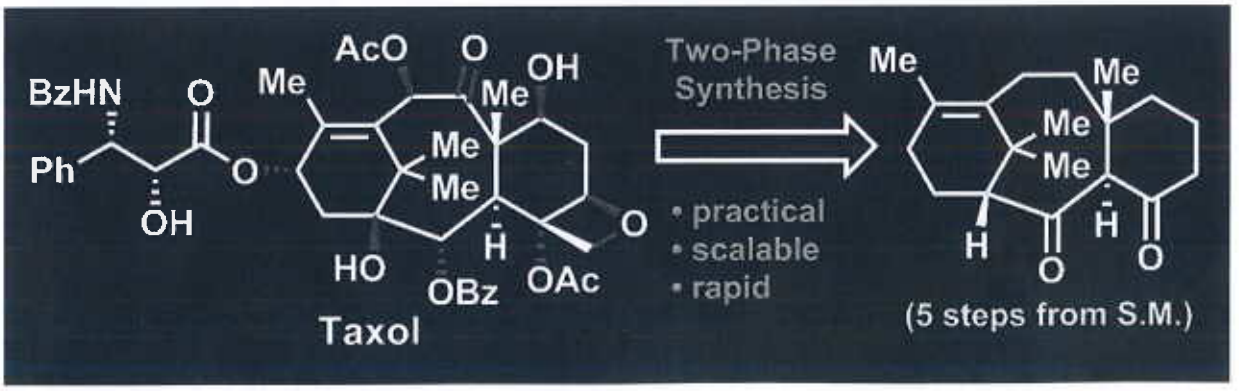
The beauty and science of the field of the total synthesis is one that is the manifest itself in the unpredictability and new things that one discover because we just don't understand the fully the language of molecules. There are couple recent examples that excite me. In this particular case because of rare natural products, very little of it can be made, so if you want to turn a molecule like this into a potential medicine the only way you could actually do that would be to make a lot of it.

In my postdoctoral research, my research was focused on the development of the total synthesis of natural products containing amino acids and also development of the new methodology.

My general research agenda is to investigate way to construction of complex natural product which is containing amino acid. Because, if you think about the most useful bond that anyone makes anywhere on earth, if you think about the bond that is being made 50 million times a minute as we speak, it's the amino acid. Amino acids are everywhere and we can't escape them. Therefore, what's exciting about this to me is the application to society by development of amino acid chemistry.

1. Total Synthesis of Taxol

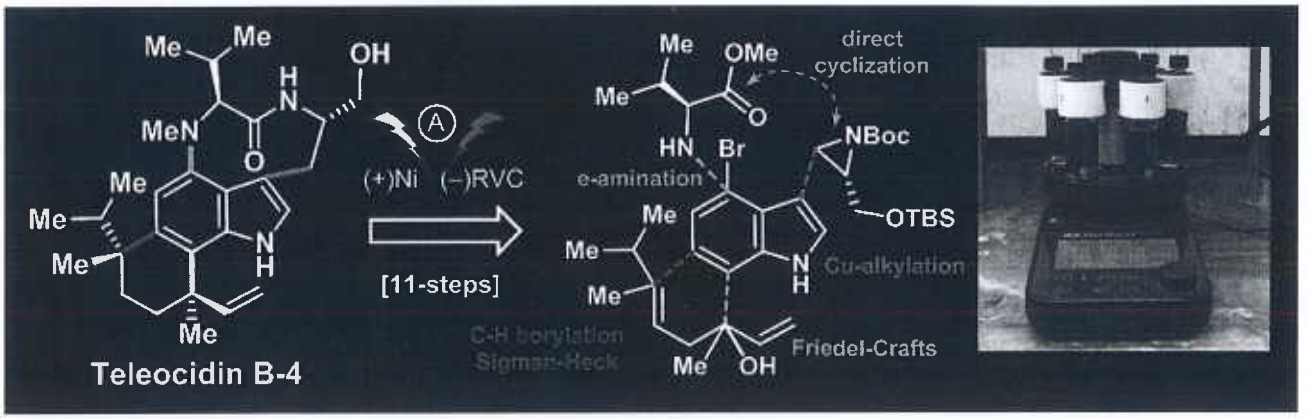
I have engaged the total synthesis of taxol. Taxol was isolated from *Taxus brevifolia*, which has miraculous anti-cancer activity. The complex structure and significant biological activities of Taxol have drawn much attention from synthetic chemists. Since 1994, more than 10 groups have accomplished the total synthesis of taxol and formal synthesis of taxol. However, efficient and scalable strategy such as a two-phase synthesis has not yet been reported. Therefore, we initiated a taxol project, which would also be applicable to related natural products. Recently, we have developed the two-phase synthesis strategy.



(manuscript in preparation)

2. 11-step Total Synthesis of Teleocidins B1-B4

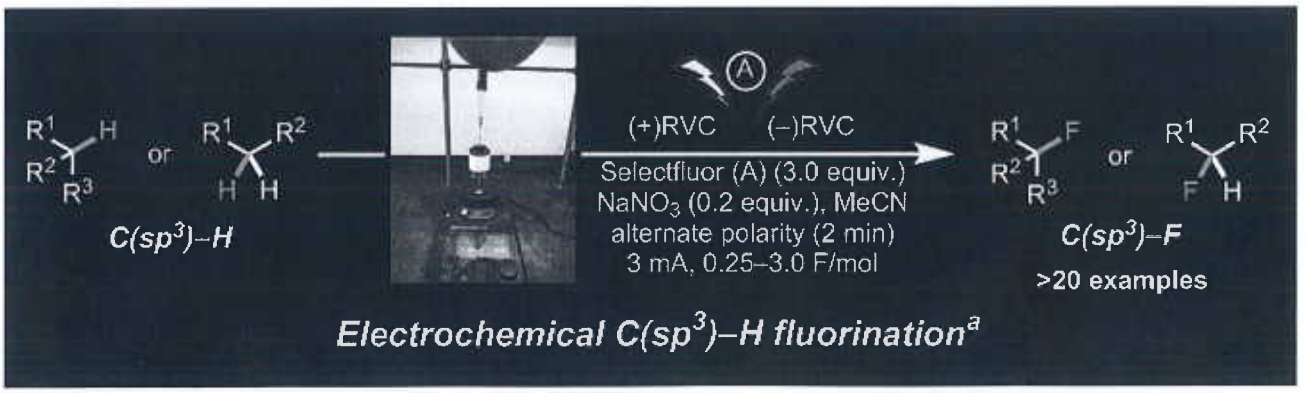
In another project, I have developed a unified and modular approach to the teleocidin B family of natural products in 11 steps and features an array of interesting strategies and methods. Indolactam V, the known biosynthetic precursor to this family, was accessed through electrochemical amination, Cu-mediated aziridine opening, and a remarkable base-induced macrolactamization. Guided by a desire to minimize concession steps, the tactical combination of C−H borylation and a Sigman−Heck transform enabled the convergent, stereocontrolled synthesis of the teleocidins.



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

3. Electrochemical C(sp3)–H Fluorination

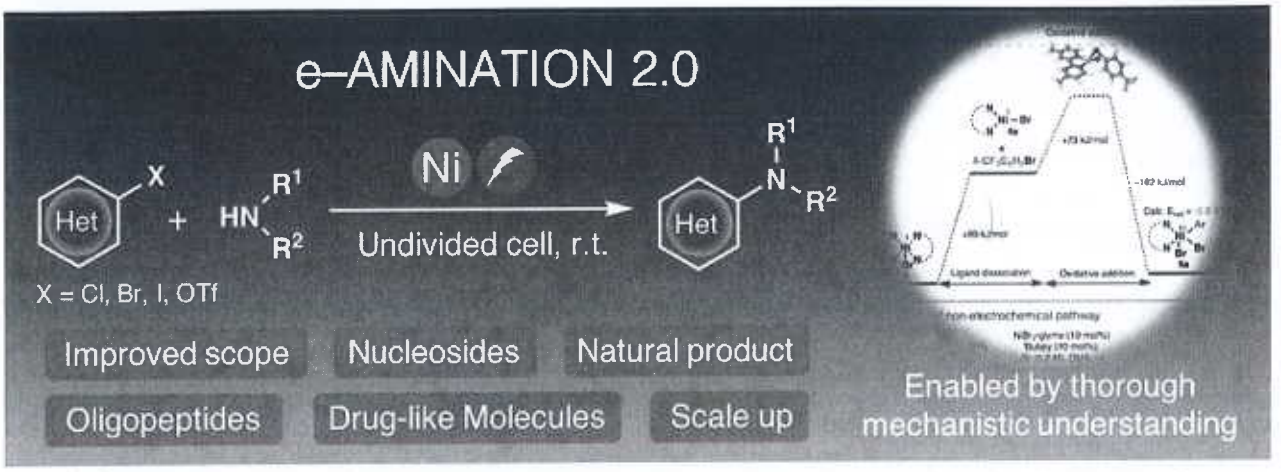
In one of the projects, I have investigated the way to fluorination by electrochemistry which can be sustainable strategy. As part of this project, I have devised a scalable, mild and practical reaction condition. The scope has been explored across arange of substrates bearing numerous types of functionalgroups and the ease of scale-up is evidenced by the 100-gram scale fluorination of a valine derivative. As electro-chemical functionalization processes become more main-stream, it is likely that this method will find use alongsideanalogous C–H oxidation processes for both building-blockdiversification and metabolic prediction.



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(sp^3)–H Fluorination"
Synlett **2019**, *30*, 1178-1182 DOI: 10.1055/s-0037-1611737

4. Electrochemical Ni-catalyzed Aryl Amination (2nd generation)

In another direction, I have investigated the way to Ni-catalyzed aryl amination by electrochemistry. As part of this project, I have investigated ligands for Ni catalyst and also I have improved scope limitation. Eventually, I found that the use of electron rich amidine ligand was crucial for amination of Bromo-indole and amino acid.



Yu Kawamata, 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. DOI: 10.1021/jacs.9b01886

5. Electrochemical Ni-catalyzed Aryl Amination (1st generation)

In one of the projects, I have developed the way to Ni-catalyzed Aryl Amination (1st generation). As part of this project, I have improved the scope limitation including hetero aryl bromide which is basically difficult to use for typical Buchwald–Hartwig–Ullmann type amination.

Along with amide bond formation, Suzuki cross coupling, and reductive amination, the Buchwald–Hartwig–Ullmann type amination of aryl halides stands as one of the most employed reactions in modern medicinal chemistry. The work herein demonstrates the potential of utilizing electrochemistry to provide a complementary avenue to access such critical bonds using an inexpensive nickel catalyst under mild reaction conditions. Of note is the scalability, functional group tolerance, rapid rate, and the ability to employ a variety of aryl donors (Ar−Cl, Ar−Br, Ar−I, Ar−OTf), amine types (primary and secondary), and even alternative X−H donors (alcohols and amides).

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