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Junpei Matsuoka

Total Synthesis of Indole Alkaloids

Based on Direct Construction of Pyrrolocarbazole Scaffolds via Gold-Catalyzed Cascade Cyclizations

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Based on Direct Construction of Pyrrolocarbazole Scaffolds via Gold-Catalyzed Cascade Cyclizations

Doctoral Thesis accepted by
Kyoto University, Kyoto, Japan

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Supervisor's Foreword

It is a great pleasure to introduce Dr. Junpei Matsuoka's thesis work on the Springer Thesis Prize as an outstanding original doctoral work. Dr. Matsuoka graduated from Meijo University in March 2016. In April 2016, he entered the Graduate School of Pharmaceutical Sciences, Kyoto University, and obtained his Ph.D. degree in my group in March 2020.

In recent years, diversity-oriented total synthesis of natural products based on direct construction of the core structures has been recognized as an important subject in organic and medicinal chemistry. The main part of Dr. Matsuoka's doctoral study is diversity-oriented total synthesis of dictyodendrins using a gold-catalyzed cascade reaction for the construction of the core structure, the pyrrolo[2,3-*c*]carbazole scaffold. After succeeded in the key cascade reaction, he faced difficulty in introduction of the requisite substituents into the resulting electron-rich pyrrolocarbazole scaffold. He suffered from the low reactivity of the Boc-protected pyrrolocarbazole and instability of the corresponding unprotected derivate which readily underwent rearrangement and polymerization. After considerable experimentations, he fully exercised his patience to overcome this difficulty and achieved the diversity-oriented total synthesis of several dictyodendrins based on late-stage functionalization. He published these significant results in *Angewandte Chemie* in 2017 and *Chemistry European Journal* (CEJ) in 2020 as the first author. Notably, it has been confirmed that the CEJ paper has been accepted on the cover page, and the profile of the research team is going to be introduced. Furthermore, Dr. Matsuoka has been working on the development of the direct construction of aspidosperma alkaloids and succeeded in formal total synthesis of vindorosine, which has been published in the *Journal of Organic Chemistry*.

Dr. Matsuoka has outstanding ability to complete natural product synthesis. The difficulties during the total syntheses can be solved by his insight to follow the reaction and logically analyze the experimental results, as well as the mental and physical strength. He was selected for the JSPS research fellowship for Young Scientists and Young Researchers Overseas Challenge Program and won some important awards such as the Kansai Branch Award, the Pharmaceutical Society of Japan (PSJ), for Young Scientists.

His thesis study has shown that gold-catalyzed cascade cyclizations have a significant power for direct construction of the core structures of biologically active alkaloids, which accelerates their total syntheses and medicinal applications. I hope his outstanding thesis will contribute to synthetic research of many readers.

Kyoto, Japan
July 2020

Prof. Hiroaki Ohno

List of Publications

This study was published in the following papers.

Chapter 2.

Total Synthesis of Dictyodendrins by the Gold-Catalyzed Cascade Cyclization of Conjugated Diynes with Pyrroles Junpei Matsuoka, Yuka Matsuda, Yuiki Kawada, Shinya Oishi, Hiroaki Ohno *Angew. Chem. Int. Ed*. **2017**, *56*, 7444−7448.

Total Synthesis of Dictyodendrins A–F by the Gold-Catalyzed Cascade Cyclization of Conjugated Diynes with Pyrroles Junpei Matsuoka, Shinsuke Inuki, Yoichi Miyamoto, Mayumi Otani, Masahiro Oka, Shinya Oishi, and Hiroaki Ohno *Chem. Eur. J. in press.* (https://doi.org/10.1002/chem.202001950).

Chapter 3.

Construction of the Pyrrolo[2,3-*d*]carbazole Core of Spiroindoline Alkaloids by Gold-Catalyzed Cascade Cyclization of Ynamide Junpei Matsuoka, Hiroshi Kumagai, Shinsuke Inuki, Shinya Oishi, Hiroaki Ohno *J. Org. Chem.* **2019**, *84*, 9358–9363

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