Synlett J. Deng, Y. Tang Cluster

Cluster Preface: Biomimetic Synthesis

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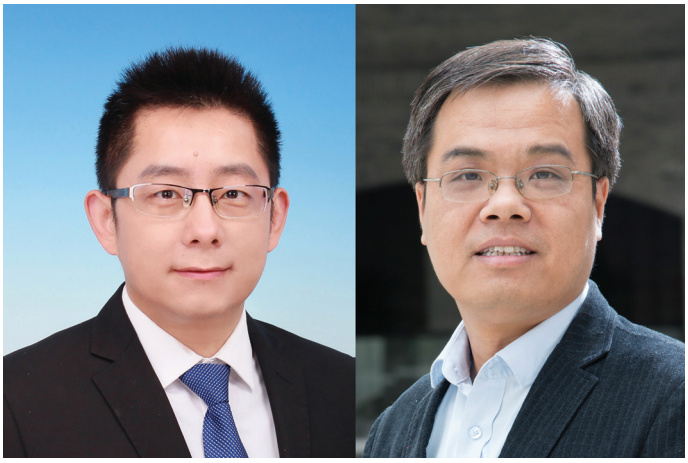

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Jun Deng (*left*) received his B.Sc. from Lanzhou University and his Ph.D. from the Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences (2014) with Professor Ang Li. After a short period of postdoctoral research in the lab of Professor Andrew Myers at Harvard University (2014–2016), he was appointed a Pioneer 'Hundred Talents Program' Researcher at Kunming Institute of Botany, Chinese Academy of Sciences in 2017. In December 2020, he moved to Nankai University where he is a professor at the College of Chemistry. He received the Thieme Journals Award (2020). His research focuses on natural product total synthesis and medicinal chemistry.

Yefeng Tang (*right*) earned his B.S. from Lanzhou University (1995–1999) and his M.S. from the Institute of Materia Medica, Chinese Academy of Medical Science (1999–2002). From 2003 to 2006, he pursued his Ph.D. under the guidance of Professor Zhen Yang and Professor Jiahua Chen at Peking University. Subsequently, he conducted postdoctoral research with Prof. K. C. Nicolaou at The Scripps Research Institute between 2006 and 2009. In 2010, he commenced his independent career at the School of Pharmaceutical Sciences, Tsinghua University, where he is now a tenured professor. His primary research interests encompass the total synthesis of natural products, the development of synthetic methodologies, and the discovery of antiviral and anti-aging drugs.

Since the disclosure of Robinson's landmark three-step, one-pot synthesis of tropinone in 1917,[1] the biomimetic synthesis of natural products has evolved into a prominent research area of organic synthesis. The essence of biomimetic synthesis lies in strategically emulating the inherent biosynthetic pathways of natural products in laboratory settings, leveraging either existing or newly developed synthetic tools. From a synthetic point of view, biomimetic synthesis has been recognized for its remarkable ability to simplify the synthetic processes toward complex natural targets. Moreover, its biomimetic nature offers some unique opportunities that are otherwise inaccessible through conventional approaches. For example, it enables facile access to a collection of biosynthetically related yet structurally diverse natural products, it provides valuable insights into the biosynthetic pathways of the obtained targets, and it can also lead to the discovery of some low-abundance or fleeting natural products that may be easily overlooked by traditional methods.[2]

To formulate a sound biomimetic strategy, researchers need to dissect the plausible biosynthetic pathways of the desired targets. However, inspiration from nature does not guarantee the successful realization of biomimetic syntheses of natural products. Instead, it necessitates the orchestrated collaboration of bio-inspiration, rational design, well-executed experiments, and even serendipitous discoveries. In essence, the biomimetic synthesis of natural products represents one of the most sophisticated scientific endeavors that embodies the harmonious convergence of human ingenuity and nature's creativity.

Over the past decades, significant strides and achievements have been made in the field of biomimetic synthesis of natural products, as witnessed by the growing numbers of publications on this subject. To encapsulate and disseminate the recent advances in this field, *Synlett* has convened a *Cluster* focused on the topic of biomimetic synthesis of natural products. This *Cluster* comprises four research articles and six accounts, encapsulating a diverse array of biomimetic synthetic endeavors.

A bioinspired formal synthesis of the montanine-type Amaryllidaceae alkaloid pancracine through selective hydrogenation of a 3-arylindole derivative has been disclosed by Qi and co-workers.[3] Meanwhile, the first total syntheses of the C4-hydroxylated securinega alkaloids 4α-hydroxyallosecurinine and securingine F have been achieved by Han and co-workers, featuring light-mediated HAT-based epimerization and skeletal rearrangement as the key elements.[4] Ishikawa and co-workers achieved the collective

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and efficient asymmetric total syntheses of five β-carboline-type monoterpenoid indole alkaloid glycosides, employing a series of bioinspired reactions developed to provide different alkaloid skeletons.[5] Practical and scalable enantioselective total syntheses of the marine anticancer sesquiterpene quinone meroterpenoids (+)-dysidavarones A–C have been accomplished by Lu and co-workers.[6] Furthermore, She, Li and co-workers have summarized the recent progress on the biomimetic synthesis of gymnotheligans based on their plausible biogenetic pathway proposal.[7] Han and co-workers summarized their latest advances on the development of novel biomimetic catalysts/catalytic systems inspired by cytochromes P450,[8] whilst Hu and co-workers have described their recent progress on the application of biomimetic dimerization strategies in the total syntheses of linderaspirone A, bi-linderone, parvistemin A, (±)-diperezone, scabellone B, and spiroxins A/C/D.[9] Additionally, Hong and co-workers have provided an overview of their biomimetic endeavors toward the macrocarbocyclic natural products, chejuenolides A–C.[10] Vincent and co-workers have reported their long journey toward the total synthesis of the mavacuran alkaloids and some highly complex natural bis-indoles.[11] Last, and by no means least, Tang and co-workers have summarized the guidance provided by quantum chemical calculations on the biomimetic syntheses of polycyclic marine furanocembrane derivatives.[12]

The elegant research showcased in this *Cluster* exemplifies the cutting-edge advancements on the biomimetic synthesis of natural products. The sophisticated orchestration of biomimetic and rationally designed transformations in these studies not only unveil the inherent wisdom in nature's biosynthesis, but also highlight the exceptional expertise of researchers in organic synthesis. Looking forwards, contemporary organic synthetic chemistry is experiencing a paradigm shift in both research philosophy and methodology, driven by the significant progress in related research areas and technologies such as synthetic biology, artificial intelligence for chemistry, and automated synthesis. Undoubtedly, the biomimetic synthesis of natural products will also benefit from this progress and more exciting discoveries and innovations are to be anticipated in this field in the future.

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Conflict of Interest

The authors declare no conflict of interest.

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