Young Career Focus: Dr. Lei Wang (Institute of Medicinal Plant Development, Chinese Academy of Medical Sciences and Peking Union Medical College, P. R. of China)

Background and Purpose. SYNFORM regularly meets young up-and-coming researchers who are performing exceptionally well in the arena of organic chemistry and related fields of research, in order to introduce them to the readership. This Young Career Focus presents Dr. Lei Wang (Institute of Medicinal Plant Development, Chinese Academy of Medical Sciences and Peking Union Medical College, P. R. of China).

Biographical Sketch

Dr. L. Wang

Lei Wang was born in Anhui (P. R. China). He received his B.S. degree in traditional Chinese medicine from the Jilin Agricultural University (P. R. China) in 2005. Then, he started his studies in natural product chemistry and obtained an M.S. degree in 2008 from the Institute of Materia Medica, Chinese Academy of Medical Sciences & Peking Union Medical College (CAMS & PUMC, P. R. China) under the guidance of Professors Ruoyun Chen and Dequan Yu. He received his Ph.D. in organic and medicinal chemistry in 2013 at the National University of Singapore (Singapore) with Prof. Jian Wang. During his Ph.D. studies, he focused his research on C–H activations and enamine chemistry and developed a series of novel reactions to synthesize heterocycles which included coumarins, benzazepines, pyrazoles, and 1,2,3-triazoles. Then he began postdoctoral research at the RWTH–Aachen University (Germany) in Prof. Dieter Enders's group, where he worked on NHC catalysis, supported by the Alexander von Humboldt Foundation. After working as a senior research fellow at the National University of Singapore, he joined the Institute of Medicinal Plant Development, CAMS & PUMC as an associate professor in 2017. Currently, Dr. Wang focuses his research on asymmetric catalysis, medicinal chemistry and natural product chemistry. He was awarded the Natural Science Prize of Ministry of Education of China (Second Class) in 2013 and the Alexander von Humboldt Scholars from Germany in 2016. In 2019, he received the Thieme Chemistry Journals Award.

INTERVIEW

SYNFORM *What is the focus of your current research activity?*

Dr. L. Wang The goal of my group is to develop novel synthetic transformations via organocatalysis/transition-metal catalysis and apply these methods to bioactive complex molecule synthesis and late-stage functionalization of natural products and marketed drugs. The ultimate goal is to establish efficient synthetic pathways to assemble bioactive molecule derivatives and to increase the probability of success in clinical trials. Additionally, we are interested in developing synthetic methodologies to construct axially chiral compounds, which are widespread in biologically active molecules.

SYNFORM *When did you get interested in synthesis?*

Dr. L. Wang I became interested in organic synthesis during my Bachelor's studies at Jilin Agricultural University. I was captivated by the story of the discovery of artemisinin and the assembly of artemisinin derivatives via organic synthesis to reduce the mortality rates for patients suffering from malaria. I was so curious about why natural products could play a magic role in curing diseases and how synthetic chemistry could enhance the curative effects. Then in my Master's studies at the Institute of Materia Medica, CAMS & PUMC, I was fortunate to work on natural product chemistry to further understand the magic role of natural products in drug discovery, nutrition, cosmetology, and applied chemistry. During this period, I was also attracted by Prof. Dequan Yu's seminar about bioactive natural product structure modifications and derivative synthesis, which helped me to understand the importance of organic synthesis in drug discovery. Thus, I chose to perform my Ph.D. research in organic and medicinal chemistry at the National University of Singapore, where I devel-

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oped synthetic methods to construct versatile novel bioactive molecules via C–H activations and enamine catalysis. Then I moved to RWTH–Aachen University for postdoctoral studies under the supervision of Prof. Dieter Enders, where I focused on the construction of chiral bioactive molecules using various organocatalysts.

SYNFORM *What do you think about the modern role and prospects of organic synthesis?*

Dr. L. Wang I believe that organic synthesis belongs to the fundamental science lying between physics and biology. Organic synthesis, the art and science of constructing novel substances, plays a central role in materials science, agricultural chemistry, environmental science, especially in medicinal chemistry and pharmaceutical industry. Organic synthesis, in some sense, forms the bottleneck of the construction of new valuable bioactive molecules. Thus, I think one important continuing role is to explore atom- and step-economic methods for bioactive molecule synthesis, together with the construction and development of novel lead compounds. Within the rapidly growing realm of organocatalysis, domino/cascade reactions from simple substrates for the construction of bioactive complex molecules have emerged as important routes to achieve sustainable synthesis. Another goal of organic synthesis is to develop novel and simple synthetic methods that are suitable for mass production, with the lowest cost possible. The potential methods for mass production should be scrutinized for both safety and environmental considerations, and involve multi- and trans-disciplinary collaborations incorporating organic syntheses, bioassays, and clinical trials.

SYNFORM *Could you tell us more about your group's areas of research and your aims?*

Dr. L. Wang Inspired by Nature's success in generating bioactive molecules in an efficient and environmentally friendly way, one major focus of my research is to synthesize bioactive molecules with environmental friendliness and operational simplicity. We employed organocatalysis for this purpose from the start of my independent academic career in 2017. Recently, we have developed some green methodologies to assemble heterocycles that were suitable for mass production with the lowest cost possible and optimization of lead compounds. We have also employed NHC catalysis to synthesize a series of heterocycles embedded with an oxindole moiety together with using the diversity-oriented synthetic strategy as a tool for the discovery of novel biologically active small molecules for further clinical development. Moreover, transdisciplinary collaborations to achieve hit compounds among our organic syntheses with bioassays and clinical trials are also continuing in my lab.

SYNFORM *What is your most important scientific achievement to date and why?*

Dr. L. Wang Our recent progress in organocatalysis with environmental friendliness and operational simplicity is something I consider so important (*Commun. Chem.* **2019**, *2*, 69). This triazene–alkyne cycloaddition produces reactive triazene intermediates, which readily participate in the cycloaddition reactions with terminal/internal alkynes, thus assembling densely substituted 3-trifluoromethylpyrazole scaffolds with high efficiency (Figure 1). The cycloaddition strategy is also extended to enable late-stage functionalization of pharmaceuticals, such as anti-cancer drug (erlotinib), anti-HIV drug (efavirenz), and antihypertensive drug (pargyline). The protocol also exhibits a remarkable broad scaffold diversification scope to embed 3-trifluoromethylpyrazole into various kinds of bioactive compounds, ranging from pharmaceutically relevant molecules and natural products to a panel of bioactive heterocycles, such as paclitaxel, hydroxycamptothecin, fluorouracil, flavonoids, coumarins, alkaloids and so on. Considering the important role of COX inhibition in antiplatelet therapy, we also developed the synthesis of a novel drug-like platelet aggregation inhibitor using this protocol on a ten-gram scale without erosion of the yield. Due to its ease of operation, high efficiency, and environmental friendliness, this synthetic strategy will significantly accelerate the efficiency of related lead-compound and drug-discovery processes.

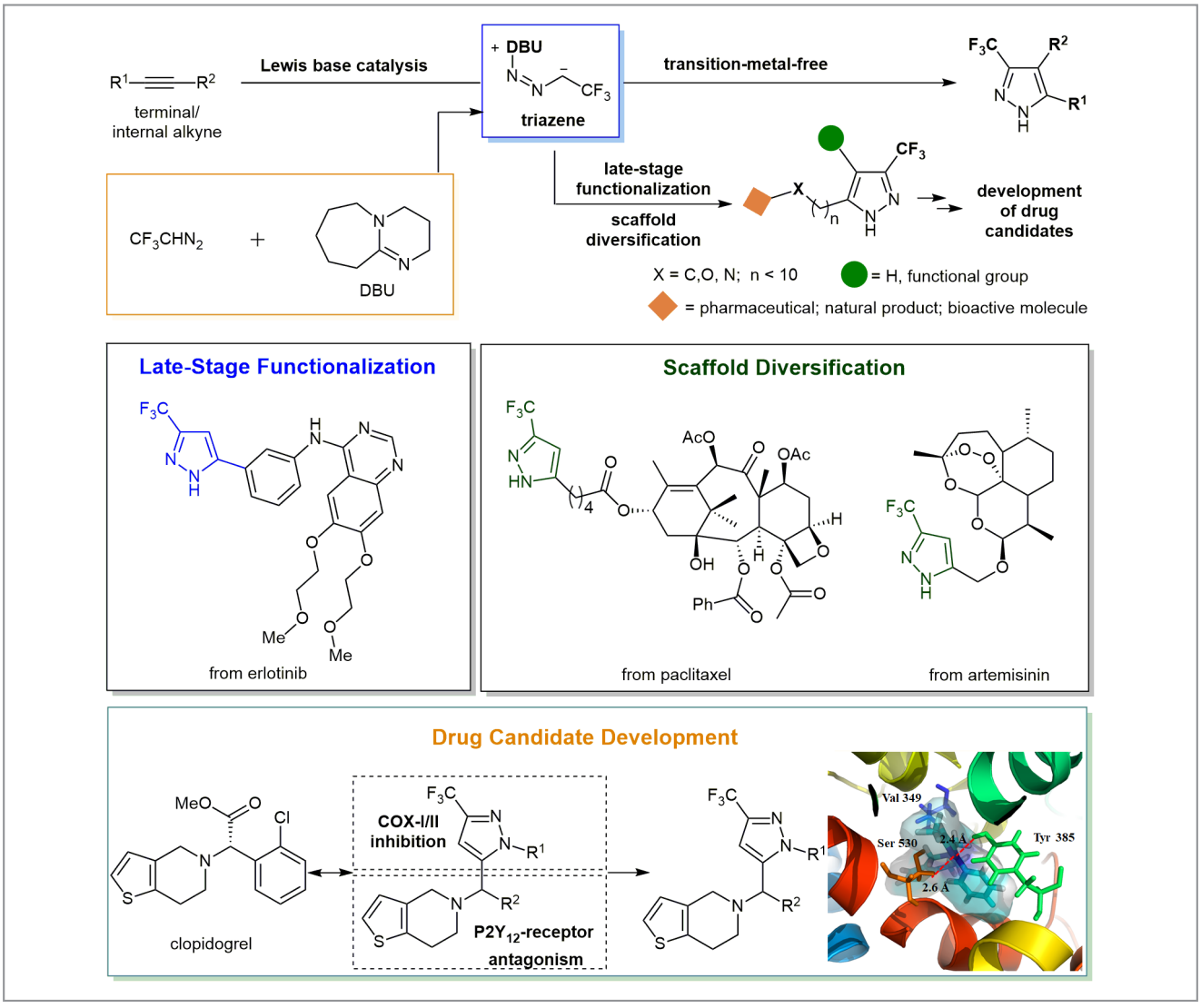

Figure 1 Triazene–alkyne cycloaddition for the assembly of 3-trifluoromethylpyrazoles, late-stage functionalization, scaffold diversification, and novel drug candidate development