

Gold(I)-Catalyzed Polycyclization of Linear Denediynes to Seven-Membered-Ring-Containing Polycycles via Tandem Cyclopropanation/Cope Rearrangement/C–H Activation

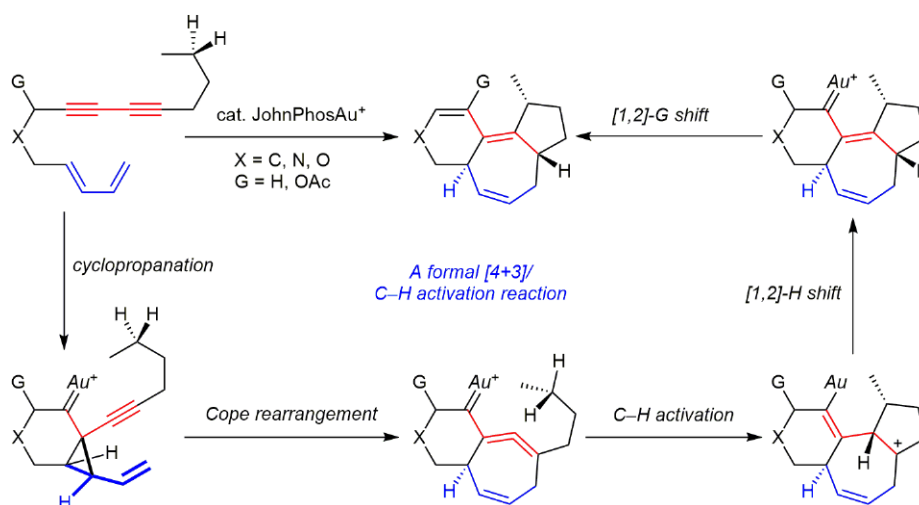
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■ Daphnane and tigliane diterpenes, such as resiniferatoxin and phorbol, respectively, are widely found in natural products and many bioactive compounds. However, the synthetic efficiency for the construction of the fused 5,7,6-tricyclic skeleton of these diterpenes by traditional step-by-step strategy is usually low (for a list of references see the original paper). Recently, a research team led by Professor Zhi-Xiang Yu from Peking University (Beijing, P. R. of China) discovered and developed a gold(I)-catalyzed tricyclization for the diastereoselective synthesis of the challenging fused 5,7,6-tricyclic system of the target diterpenes from linear dienediynes. This cascade reaction occurs via a multistep sequence involving intramolecular cyclopropanation of the dienediyne substrate, Cope rearrangement of the resulting alkenylalkynylcyclopropane, C–H activation based on cyclic allene C–H insertion, and two consecutive [1,2]-shift reactions to yield the target skeletons with high diastereocontrol.

“Cope rearrangement of divinylcyclopropanes is one of the most widely used reactions for the construction of seven-membered carbocycles,” said Professor Yu. “However, Cope rearrangement of alkenylalkynylcyclopropanes has rarely

been used, perhaps due to the formation of a reactive seven-membered-ring allene, which may undergo rapid dimerization to give undesired products.” He added: “By using easily prepared dienediynes as substrates, we found that the seven-membered-ring allene intermediate, which was generated in situ by the Cope rearrangement of an alkenylalkynylcyclopropane, undergoes C(sp³)-H activation of the side chain, instead of the undesired dimerization, to furnish the fused 5,7,6-tricyclic system. The present polycyclization reaction is a good example for step-economic construction of complex and challenging skeletons of important molecules from simple starting materials.”

“The present reaction is the second unexpected C–H activation reaction reported by our group,” said Professor Yu. “Previously we have developed a process for the rhodium-catalyzed allylic C–H activation/addition to alkene and used it for the synthesis of multi-substituted tetrahydropyrroles, tetrahydrofurans, and cyclopentanes bearing quaternary carbon centers (*J. Am. Chem. Soc.* **2010**, *132*, 4542; *Angew. Chem. Int. Ed.* **2011**, *50*, 2144).” Professor Yu explained: “Developing new C(sp³)-H activation reactions under mild

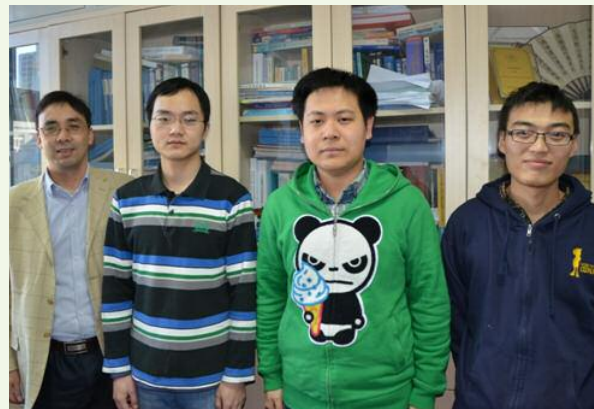


conditions to streamline organic synthesis is pursued by many leading synthetic chemists throughout the world. Although my group is not directly involved in this ‘hot’ field, we always keep an eye on its development. Our present reaction suggests that many other ‘unexpected’ C–H activation reactions are waiting for further exploration by synthetic chemists.”

One of the research interests of Professor Yu’s group is to develop new ring-formation reactions and apply these reactions to the synthesis of natural products (for a review, see: *J. Org. Chem.* **2013**, *78*, 6842). “The present polycyclization can be regarded as a formal [4+3]/C–H activation reaction,” said Professor Yu, who concluded: “In addition to developing more powerful ring-formation reactions, we are going to do more investigations on the present polycyclization. We are currently studying the detailed reaction mechanism using DFT calculations. Our next goal is to explore other chemistry of cyclic allenes.” ■

Matteo Zanda

About the authors



From left: Prof. Z.-X. Yu, P.-J. Cai, Y. Wang, C.-H. Liu

Zhi-Xiang Yu obtained his PhD from the Hong Kong University of Science & Technology (P. R. of China) in 2001. After a three-year postdoctoral study at University of California, Los Angeles (USA), he joined the faculty of Peking University (P. R. of China) as an associate professor in 2004 and was promoted to full professor in 2008. With a research philosophy of “chem-is-try, computationally and experimentally”, his laboratory focuses on the application of computational and synthetic organic chemistry to study reaction mechanisms, develop new reactions and catalysts, and apply the new reactions discovered from his group to synthesize natural and non-natural products.

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