

Efficient and collective total synthesis of natural products via radical cascade reactions

Subject Code: B02

With the support of the National Natural Science Foundation of China, the research team led by Prof. Qin Yong (秦勇) at Sichuan University accomplished a collective synthesis of 33 monoterpene indole alkaloids that belong to four families, by developing new photoredox-initiated radical cascade reactions. The corresponding results were recently published in *Chem* (2017, 2: 803–816).

Structurally complex and diverse natural products have been important sources of new drugs. A long-standing challenge in drug screening is how to secure various natural products with structural specificity. Traditional methods to access such molecules by isolation from natural resources are usually insufficient for the requirement of drug discovery. Natural product synthesis provided a possible solution to this issue, however, the scale of which was limited by the known organic synthetic technologies. Monoterpene indole alkaloids represent a large and unique family of natural products that are characterized by complex and diverse structures, as well as an important range of bioactivities. These features have rendered various indole alkaloids highly pursued targets for synthetic chemists.

Qin's group disclosed that under visible-light-mediated photocatalytic conditions, a nitrogen-centered radical could be generated via deprotonation and oxidization of a sulfonamide N-H bond and subsequently triggered three types of cascade reactions (intramolecular/intramolecular, intramolecular/intermolecular, and intramolecular/inter-molecular/intramolecular), thus leading to rapid assembly of the aspidosperma-, tetrahydrocarbolinone-, and corynanthe-type of skeletons (types I-III, Figure), respectively. This protocol is innovative in uncovering a new way for generating nitrogen-centered radicals directly from sulfonamide N-H bonds under mild conditions and in developing a new method for the preparation of chiral indolines by reversing the conventional reactivity between two electron donating amine and enamine groups. Additionally, this cascade introduces complexity and functionality into products with excellent and precise control of chemo-, regio-, and diastereoselectivity, which were typically difficult to achieve in radical reactions. More importantly, efficiently collective synthesis of indole alkaloids has thus been accomplished by employing this green and scalable method as key step, which serves as a good example for scalable preparation of natural product libraries with structural diversity.

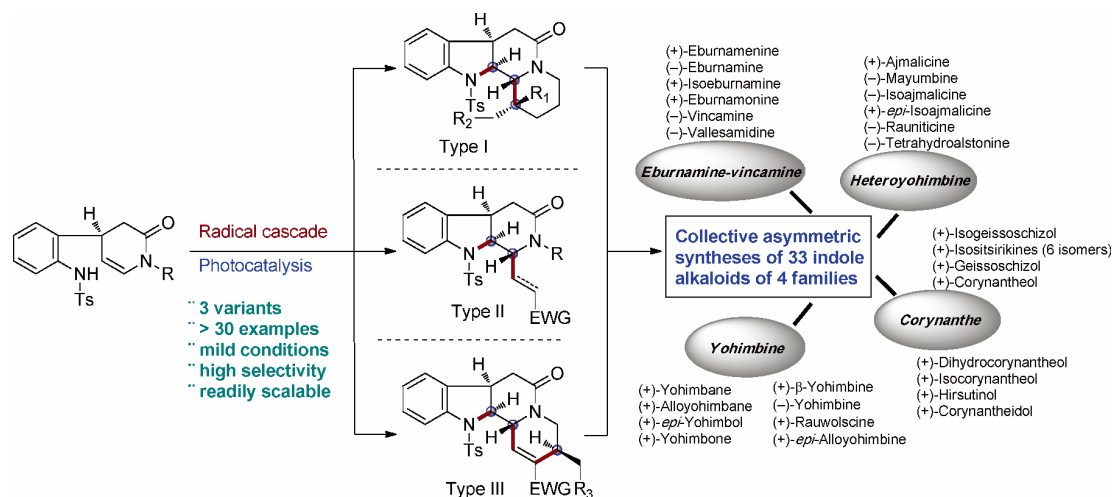


Figure Collective synthesis of natural products via radical cascade reaction.