New way of synthesizing organic chemicals mimics nature

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Organic chemists have found a new way of synthesizing multiple complex organic molecules that until now have needed to be synthesized using time-consuming methods. The new strategy, which mimics natural biosynthesis methods, could provide a way to speed up the synthesis of chemicals for use in the laboratory and for testing for possible therapeutic effects.

Chemists can synthesize almost any complex organic chemical in small quantities in the laboratory, but the process can be extremely time consuming and expensive, and difficult or impossible to translate to large-scale production. It is also difficult to synthesize families or related molecules using traditional methods because each has to be synthesized individually.

The new method was developed by researchers from the Merck Center for Catalysis at Princeton University in the U.S., led by organic chemist David MacMillan. The strategy combines two techniques that mimic methods used by living systems to synthesize organic molecules (those based on chains of carbon atoms or carbon rings): organocascade catalysis and collective synthesis. Combining these two techniques for the first time allowed MacMillan and colleagues to considerably speed up the synthesis of a group of six related alkaloids.

The alkaloids the team manufactured were akuammicine, aspidospermidine, kopsanone, kopsinine, strychnine, and vincadifformine.

The new strategy, which the team calls “collective total synthesis,” makes it possible to synthesize useful amounts of related, complex molecules from a “common molecular scaffold,” and is much less time-consuming. The synthesis of strychnine, for example took place in only 12 stages, which is the shortest ever reported.

Traditional methods of synthesizing such chemicals have involved using chemical reactions to produce each individual intermediate and then isolating it and using the intermediate in the next reaction, and repeating this process until the target molecule is finally produced.

MacMillan said the new method represents a new way of thinking for organic chemists. Reducing the number of steps required to synthesize molecules reduces the time required and can also reduce the cost and wastage. Their approach can also produce a number of related molecules at the same time, which could reduce the time and cost of producing and testing chemicals to find the most bioactive drug candidates.

MacMillan and the team suggest the collective total synthesis strategy could be used to manufacture other families of molecules that until now have had to be synthesized individually. They say the approach of combining the two techniques of organocascade catalysis and collective synthesis could be applicable for many other groups of molecules besides alkaloids.

The paper, the first to be published describing this approach to synthesis, is published in *Nature*.

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