

A 'home run' approach: Team finds new ways to synthesize HIV inhibitor

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Seth Herzon is in his lab. Credit: Michael Helfenbein/Yale University

Yale University chemists have created a new process for synthesizing an organic, nitrogen-based compound that inhibits HIV.

The process represents a fundamentally different approach to synthesizing alkaloids, which are naturally occurring compounds that contain nitrogen. The new approach uses a set of starting materials that do not require the usual tempering of nitrogen's reactive tendencies.

"We unmask the nitrogen in the last step," said Seth Herzon, a Yale chemistry professor and co-author of a new study in the journal *Nature*. "Using this approach, we're able to streamline the synthesis in ways that are otherwise not possible. It's a huge time saver."

Co-authors on the study are former Yale postdoctoral associate Brendan Parr and Yale graduate student Christos Economou. Herzon's lab at Yale has conducted extensive research on natural products synthesis and the development of new synthetic methods.

The new process highlighted in *Nature* produces a synthetic version of the anti-HIV chemical batzelladine B, which is found naturally in a bright red sponge in the Caribbean. Batzelladine B shows promise as an inhibitor of HIV viral entry, one of the first steps in the development of HIV infections.

In this case, the researchers used aromatic nitrogen heterocycles—a less reactive material—as a starting point. This opened the way to apply novel strategies for synthesis. For example, Herzon said, his team was able to pursue a number of highly complex reactions, or transformations, within a single step of the process. One step included a cascade of 10 distinct chemical transformations.

"We went for a home-run approach," Herzon said. "Our results bring us to the natural product in a minimal number of steps."

The [process](#) might be adapted to synthesize other compounds, as well. Herzon said his team has identified at least a dozen other alkaloids as candidates, including anti-cancer, anti-microbial, and other anti-HIV compounds.

More information: A concise synthesis of (+)-batzelladine B from simple pyrrole-based starting materials, *Nature*, [DOI: 10.1038/nature14902](#)

Provided by Yale University

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