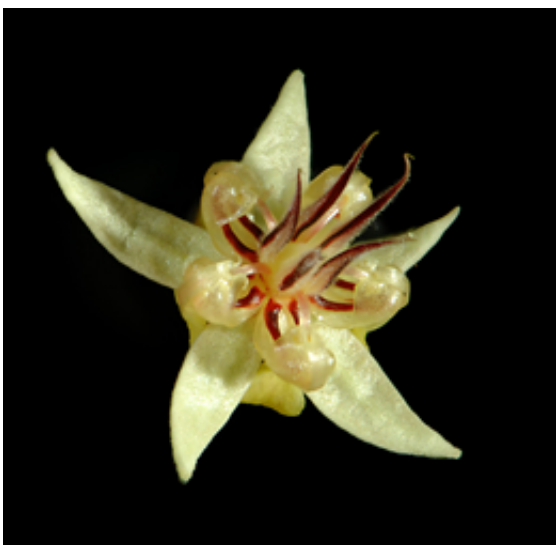


Chemists report the first total synthesis of the natural product epicolactone

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Epicolactone is produced by an endophytic fungus which grows on agriculturally important tropical plants such as the cocoa tree.

In the latest issue of the journal *Nature Chemistry* researchers led by Dirk Trauner, Professor of Chemical Biology and Genetics at LMU Munich, describe the biomimetic synthesis of epicolactone, a compound which was first isolated from an endophytic fungus. "What we have accomplished is one of the shortest and most elegant total syntheses of a natural product ever reported," says Trauner, as he and his colleagues have indeed succeeded in producing a highly complex molecular structure in a minimal number of steps. "This is actually very close to being an ideal synthesis – at least according to one of our reviewers," he

adds. The method used not only reveals how epicolactone is assembled by its fungal producer but also places the molecule in a broader biosynthetic context.

Epicolactone was first isolated in pure form in 2012. The compound is produced by the [endophytic fungus](#) *Epicoccum nigrum*, which grows on agriculturally important tropical plants such as sugarcane and the cocoa tree. From a structural point of view, epicolactone is a highly complex natural product. It contains several stereocenters and is characterized by an intricate network of interconnected rings. "We wanted to know how this very beautiful structure is put together by the organism and we wanted to apply this knowledge to the design an efficient total synthesis" says Dirk Trauner.

Simple precursor, complex product

Nothing was known about the biosynthesis of epicolactone, but the LMU team noticed similarities between its structure and the compound purpurogallin. Purpurogallin is the archetype of a whole class of natural pigments, some of which are responsible for the dark color of fermented teas and of many species of fungus. Ink made by combining iron salts with extracts from oak galls has been used for over 2000 years, and owes its brownish-black color to purpurogallin.

"The biosynthesis of purpurogallin is well understood, and this enabled us to design a scheme for the biomimetic total synthesis of epicolactone. The pathway begins with vanillyl alcohol and leads in only eight steps to epicolactone," Trauner explains. "This is yet another example of how a structurally complicated natural product is assembled from simple precursors using a reaction cascade." The synthetic pathway also gives to a related compound called isoepicolactone, which is likely to occur in *E. nigrum* as well.

The new findings make it possible to produce epicolactone in larger quantities in the laboratory. The LMU group now plans to elucidate the precise mechanism of the chemical cascade in the context of Collaborative Research Center 749 (intermediates of Molecular Transformations) with a view to understanding its wider biochemical significance.

More information: "An eight-step synthesis of epicolactone reveals its biosynthetic origin." *Nature Chemistry* (2015) [DOI: 10.1038/nchem.2336](https://doi.org/10.1038/nchem.2336)

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