Taking Risks in Complex Synthesis Design

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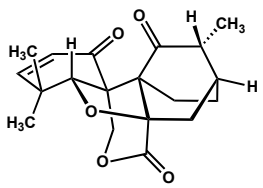
Abstract

This lecture defines risk-taking in organic synthesis as the deliberate pursuit of strategies that do not have near neighbors in the chemical literature. The key transformation in Woodward's landmark synthesis of chlorophyll, Pattenden's construction of the steroid architecture by a cascade of free radical cyclizations, Baran's concept for synthesizing the bent benzene ring of haouamine A, and Heathcock's artful, nature-inspired synthesis of the molecular skeleton of the *Daphniphyllum* alkaloids are among the achievements that demonstrate the merits of creative risk-taking in the planning and execution of organic syntheses. These examples provide a historical context for this lecture, which traces the evolution of our efforts to accomplish a concise synthesis of maoecrystal V, an anticancer metabolite from the Chinese medicinal herb *Isodon Eriocalyx*.



Maoecrystal V

In our laboratory, the intricate molecular structure of maoecrystal V stimulated diverse concepts for chemical synthesis. This lecture will describe the unpublished chemical reactions and ideas that have allowed us to reach an advanced stage on the path to an enantiospecific synthesis of maoecrystal V. A site-selective and fully stereocontrolled C–H insertion reaction and the incorporation of the atoms of a simple protecting group into an advanced intermediate for synthesis are key aspects of this work.