

In 2008, (+)-aspergillide C was isolated from a marine-derived fungus, *Aspergillus ostianus* strain 01F313, collected off the coast of Pohnpei. It was cultured as a secondary metabolite in a bromide-rich artificial seawater medium. In a biological study, (+)-aspergillide C displayed cytotoxicity against mouse lymphocytic leukemia cells (L1210) with an LD50 value of 2.0 $\mu\text{g/mL}$. Due to a limited supply of the naturally occurring compound, its synthetic production was necessary to facilitate a complete biological evaluation.

An enantioselective formal total synthesis of the cytotoxic macrolide (+)-aspergillide C has been accomplished from (S)-(–)-glyceraldehyde acetonide and the Danishefsky-Kitahara diene. Strategic transformations include a hetero Diels-Alder reaction, Ferrier-type addition, and palladium-catalyzed oxidative lactonization to set key stereocenters within the dihydropyran core, followed by fragment coupling via (*E*)-selective Julia-Kocienski olefination.