

Novel Variants of the Zwitterionic Claisen Rearrangement and the Total Synthesis of Erythronolide B

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Abstract

This dissertation describes the development of three novel variants of the zwitterionic Claisen rearrangement. Initial studies demonstrate an efficient and diastereoselective ketene-Claisen rearrangement catalyzed by metal salts. This process involves the condensation of ketenes and allylic amines to form zwitterionic enolates which undergo [3,3]-sigmatropic rearrangements to afford α,β -disubstituted- γ,δ -unsaturated amides. The scope of this chemistry is further expanded through the development of a Lewis acid-catalyzed acyl-Claisen rearrangement which employs acid chlorides as ketene surrogates. Based on these studies, a new tandem acyl-Claisen rearrangement for the construction of structurally complex 1,7-dioxo-acyclic architectures is achieved. The versatility of this tandem transformation for macrolide antibiotic synthesis is demonstrated through a concise total synthesis of erythronolide B, in 24 linear steps.

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