

Stony Brook University The Graduate School

Doctoral Defense Announcement

Abstract

I. Asymmetric Synthesis of *Anti*-, *Anti*-Stereotriad Building Blocks for Polypropionate Natural Products II. Synthesis Study towards C9-C14 moiety of (+)-Discodermolide III. One-Pot Asymmetric Synthesis of Secondary Propargyl Alcohols

By

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I. Polypropionate subunits are present in a great number of biological active natural products such as antibiotics, antitumors, antifungals, or antiparasitics. A widespread strategy to synthesize these structures involves the disconnection of polypropionate chains into shorter subunits, such as stereotriad building blocks bearing alternate methyl and hydroxyl groups. Starting from inexpensive, commercially available achiral starting materials, a powerful protocol was developed to construct *anti*-, *anti*-stereotriad building blocks. With further modifications, the 3-hydroxy-2,4,6-trimethylheptanoic acid (TMHEA) segment of Callipeltin A and the Segment B2 of Miyashita's total synthesis of Scytophycin C was synthesized from these stereotriads.

II. (+)-Discodermolide, a marine sponge natural product that stabilizes microtubules and maintains activity against multidrug resistant cell lines, is currently in clinical trials as an anticancer drug developed by Novartis Pharmaceuticals. Most of the completed total syntheses of (+)-discodermolide have relied on the Roche ester as the source of chirality and enantioselective chain extensions for construction of the building blocks. In our retro-synthetic plan towards (+)-discodermolide, the disconnections at C8-C9, C14-C15 generated three fragments. While my colleagues concentrated on the C1-C8 fragment and C15-C24 fragment, my work focuses on the synthesis of the C9-C14 stereotriad moiety.

III. Chiral secondary propargyl alcohols are versatile building blocks for fine chemicals, pharmaceuticals, and natural products. A convenient method for asymmetric synthesis of secondary propargyl alcohols is highly demanded. Based on preliminary study, asymmetric synthesis of secondary propargyl alcohols in one-pot was designed and achieved by applying Zn-catalyzed enantioselective alkynylation directly with the aldehyde products of substitution reaction of methyl formate with nucleophiles. Various chiral alcohols with different substitutions have been synthesized successfully with good yield and high enantiomeric excess.

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