Stereocontrolled Total Synthesis of (–)-Myriocin

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Myriocin (**1**) was isolated as an antifungal principle from the fermentation broth of thermophilic fungal *Myriococcus albomyces* and *Myceria sterilia* in 1972. Fujita et al., who isolated **1** from *Isalia sinclairii* in 1994, have reported that it exhibits 10- to 100-fold more potent immunosuppressive activity than cyclosporine A. Recently, Kiuchi et al. have developed a novel immunosuppression drug utilizing **1** as a lead compound. The α-disubstituted α-amino acid motif has attracted much attention due to its significance in biological investigations. This remarkable bioactivity and unique structure led us to the synthetic study on **1**.

Optically active epoxide **4** was converted from symmetrical cyclohexadiene **2**, utilizing desymmetry and enzymatic kinetic resolution. The three sequential stereogenic centers of **1** were constructed by a regioselective epoxide-opening reaction and a Hofmann rearrangement. The Julia–Kocienski reaction, efficiently accomplished elongation of the side chain. We have developed an efficient stereocontrolled synthesis of (–)-**1**. Our synthetic method may be applicable to the synthesis of more structurally complex α-disubstituted-α-amino acid compounds as well as other natural and/or unnatural compounds. We are currently investigating the synthesis of (+)-myriocin and other α-disubstituted-α-amino acid compounds.