Ir-catalyzed asymmetric Tishchenko reaction and total synthesis of Cinncassin A1

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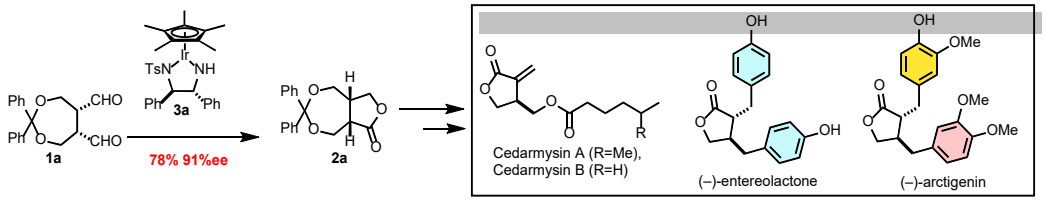
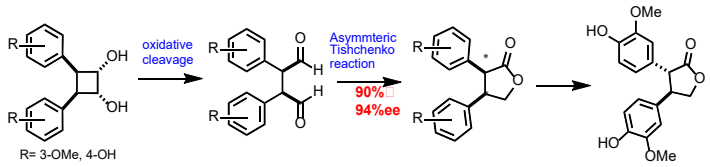
Cinncassin A_1 is a natural product isolated from *Cinnamonum cassia* Presl.,[1] and was expected to possess neuroprotective activity. The racemic synthesis of Cinncassin A_1 has been reported by Nuriye,[2] but there is no example of asymmetric synthesis. Recently, we developed a catalytic asymmetric Tishchenko reaction using Ir complex. The reaction converted *meso*-1,4-dialdehyde **1a** to chiral lactone **2a** in 78% yield with 91%ee.[3a] Using this reaction, the synthesis of cedarmycin A, B,[3a] enterolactone,[3b] (–)-arctigenin[3c] have been accomplished (Scheme 1). In this study, we investigated the asymmetric Tishchenko reaction of acyclic *meso*-1,4-dialdehyde, which was prepared for the first time by our developed method.[3d] Based on this synthetic strategy, we developed synthetic route of natural product Cinncassin A_1. The asymmetric Tishchenko reaction provided corresponding chiral lactone in 90% yield with 94%ee, and the final product was obtained with 94%ee (Scheme 2).



Scheme 1. Ir catalyzed asymmetric Tishchenko reaction



Scheme 2. Catalytic asymmetric synthesis of Cinncassin A_1

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