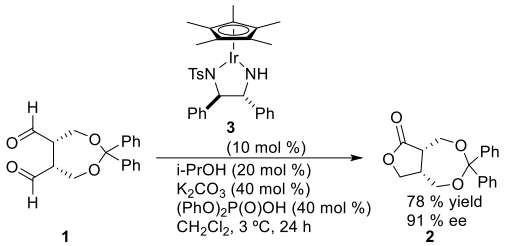
Asymmetric Synthesis of Lignan Compounds using Ir catalyzed Tischenko Reaction

(*Sanken, Osaka University*) ○Rui Jiang, Ismiyarto, Tsukasa Abe, Da-Yang Zhou, Kaori Asano, Takayoshi Suzuki, Hiroaki Sasai, Takeyuki Suzuki

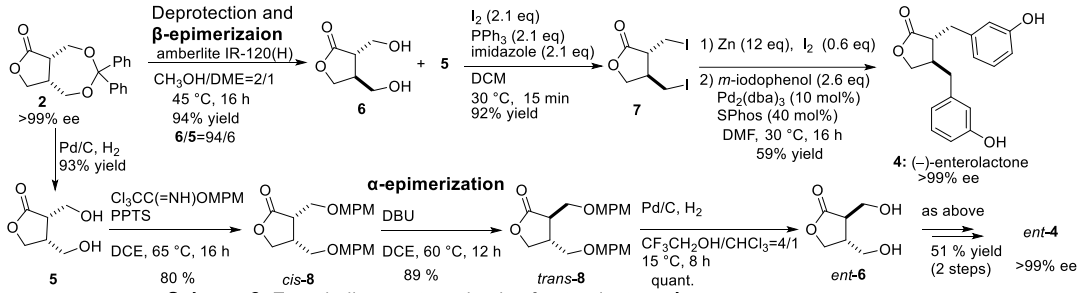
Keywords: Asymmetric Synthesis; Iridium; Lignan; Tischenko Reaction

Lignans are a class of compounds found in plants, especially fiber-rich foods such as flax seed, whole grains, berries and vegetables. A diet rich in lignans is believed to be beneficial to the health. Recently, we reported the first catalytic asymmetric Tischenko reaction using chiral Ir complex **3** (Scheme 1).



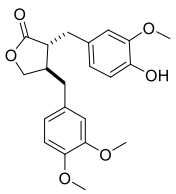
Scheme 1. First asymmetric Tischenko reaction

Lactone **2** was obtained in 78% yield with 91% ee from *meso*-dialdehyde **1**.[1,2] Herein, we report the enantiodivergent synthesis of antitumor compound enterolactone **4** by the selective epimerization (Scheme 2)



Scheme 2. Enantiodivergent synthesis of enterolactone **4**

I investigated a process starting from lactone **2**. Optically pure **2** can be obtained via the recrystallization. Deprotection of **2** under acidic condition yielded the β-epimerized *trans*-diol **6** as a main product. A subsequent Appel reaction performed on the mixture of **6** and **5** proceeded well. Finally, diiodide **7** was successfully converted to the desired (–)-enterolactone **4** via double Negishi coupling. Next, (+)-enterolactone was synthesized via α-epimerization. *cis*-Diol **5** was obtained by hydrogenolysis of lactone **2** under neutral condition and then converted to the di-MPM ((4-methoxyphenyl)methyl) ether, *cis*-**8**. Treatment of *cis*-**8** under basic condition with DBU yielded α-epimerized di-MPM ether *trans*-**8**. Removal of the MPM groups via hydrogenation gave *ent*-**6**. The obtained *ent*-**6** was treated in the same way as shown in Scheme 2 to yield (+)-enterolactone *ent*-**4** as an optically pure product. We will also discuss the asymmetric synthesis of another lignan arctigenin.



(−)-Arctigenin

1) Ismiyarto.; Kishi, N.; Adachi, Y.; Jiang, R.; Zhou, D.Y.; Asano, K.; Obora, Y.; Suzuki, T.; Sasai, H.; Suzuki, T. *RSC Adv.* **2021**, *11*, 11606. 2) A part of these results was published. See: Jiang R.; Iamiyarto.; Adachi, Y.; Abe, T.; Zhou, D.Y.; Asano, K.; Sasai, H.; Suzuki, T.; Suzuki, T. *11th CSJ Chemistry Festa,* P7-052.

© The Chemical Society of Japan