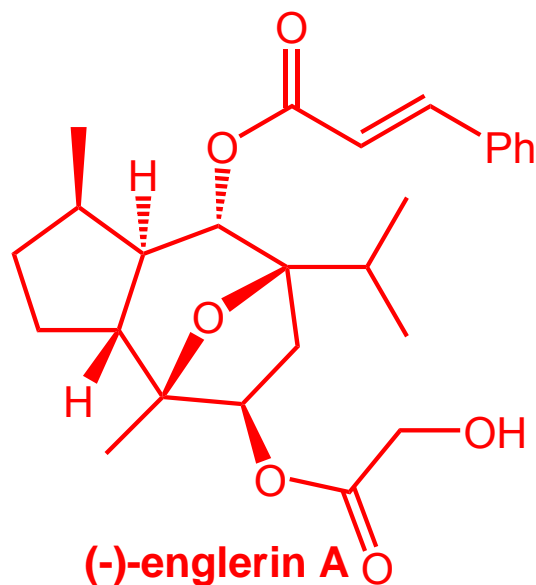


Literature Report

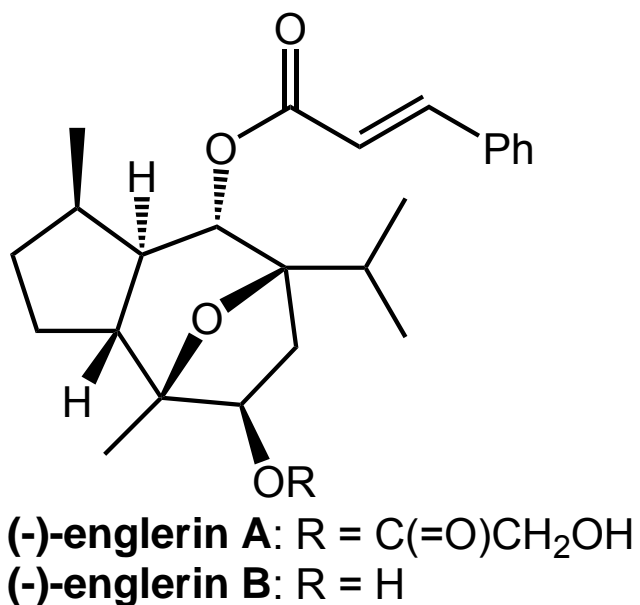
Changbin Yu 2012-09-18

检查: 黄文学

Stereocontrolled Total Synthesis of (-)-Englerin A



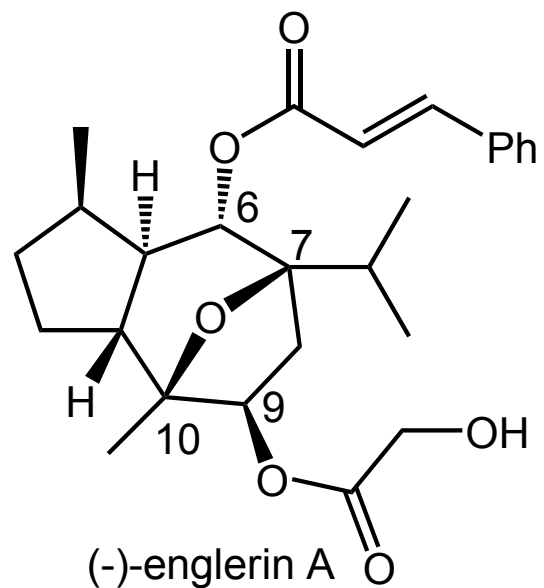
Susumi Hatakeyama* *et al.* *J. Org. Chem.* **2012**, *77*, 7364–7370.



Phyllanthus engleri (毒叶下珠)

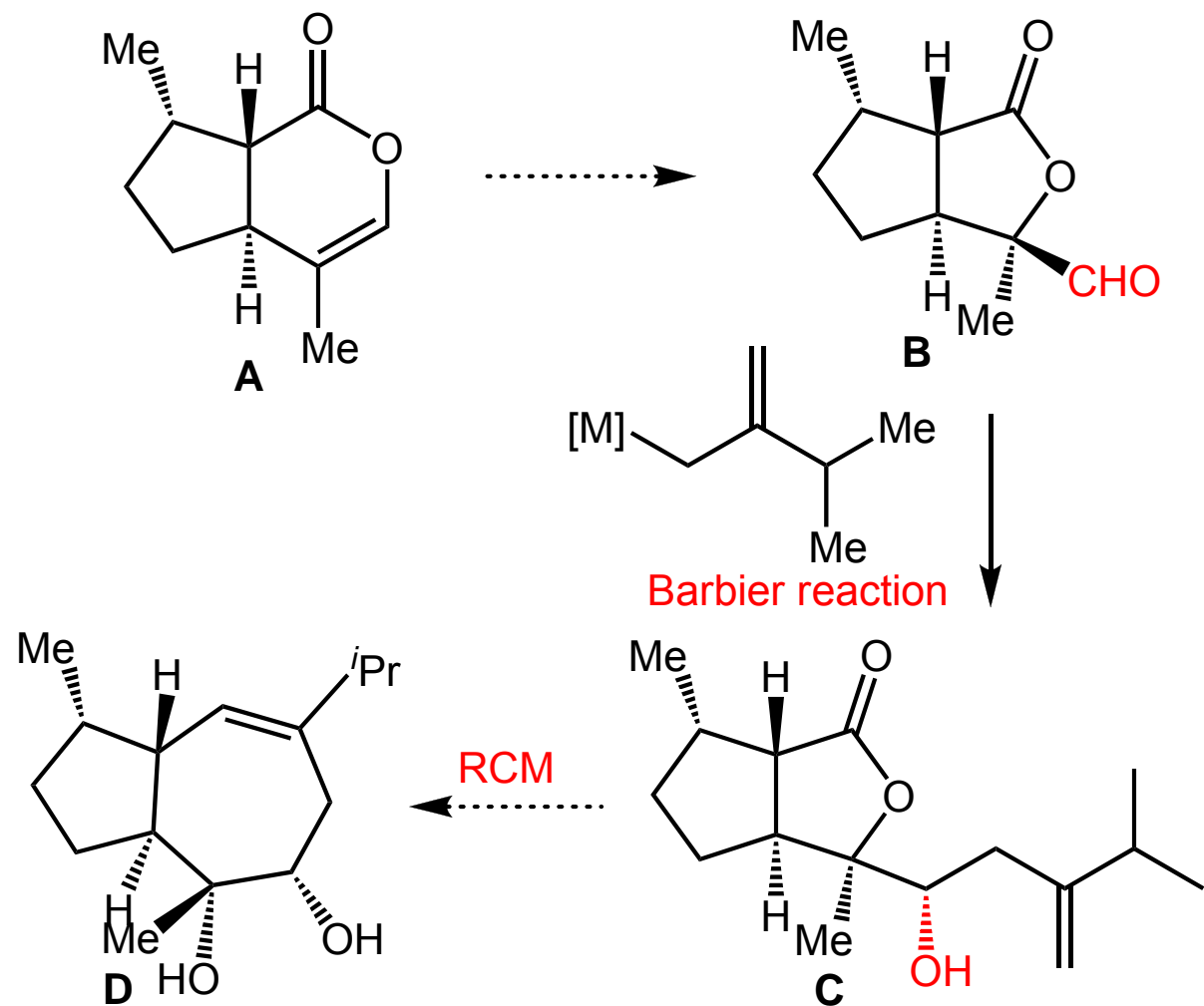
简介:

- 1、2008 年底, Beutler 小组从生长于东非 坦桑尼亚及津巴布韦的大戟属植物 *Phyllanthus engleri* 的树皮和根皮提取液中分离得到愈创木烷类(Guaienoid)倍半萜 englerin A 及其单 酯衍生物 englerin B
- 2、englerin A 对肾癌细胞表现出高效和高选择性的抑制活性

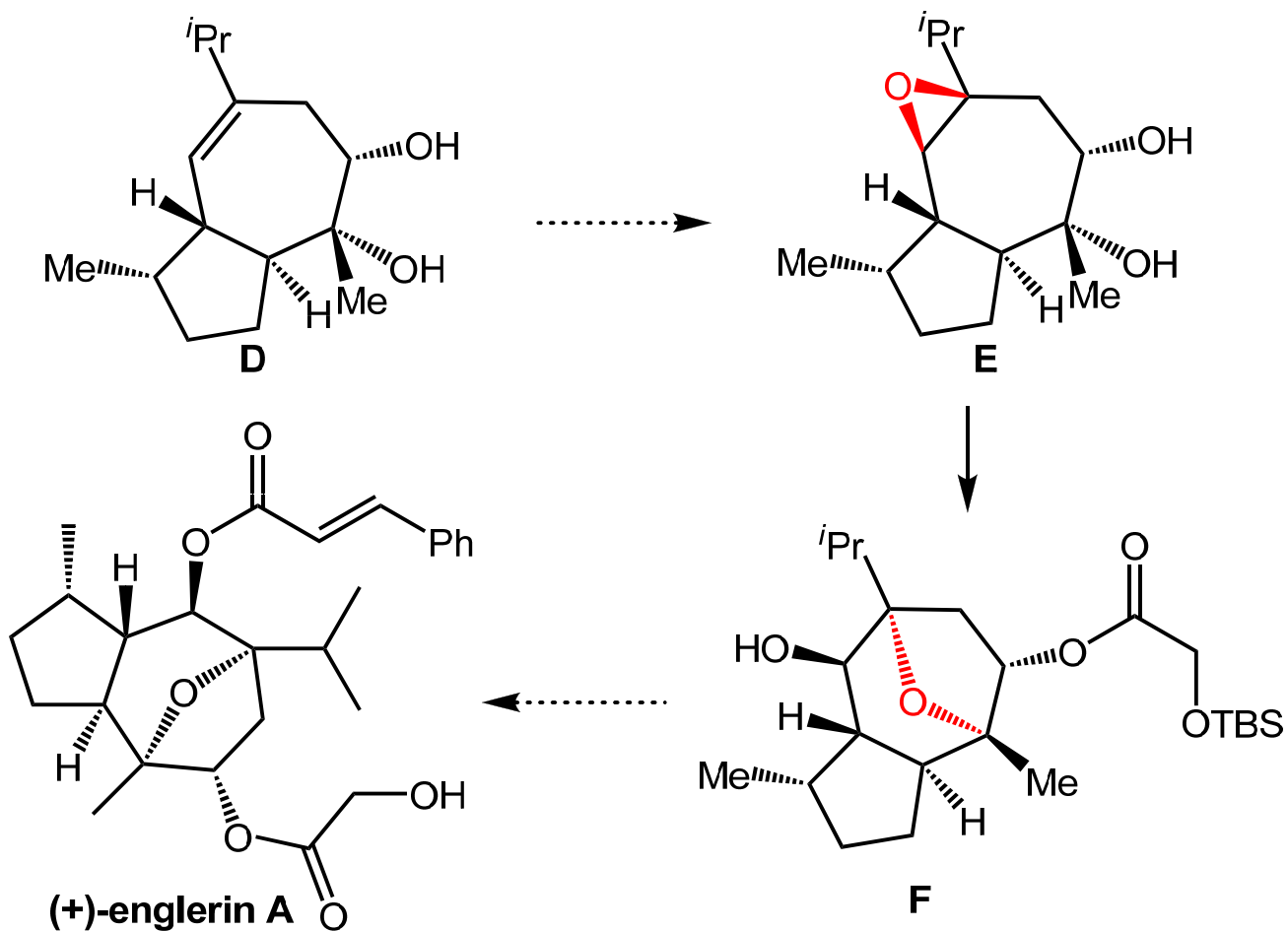


合成挑战:

- 1、反式-双环[5.3.0]骨架
- 2、在6位和9位连有对生物活性至关重要的肉桂酸和羟基乙酸侧链
- 3、含有7个连续的手性中心，其中2个为季碳
- 4、含有氧桥的并环体系

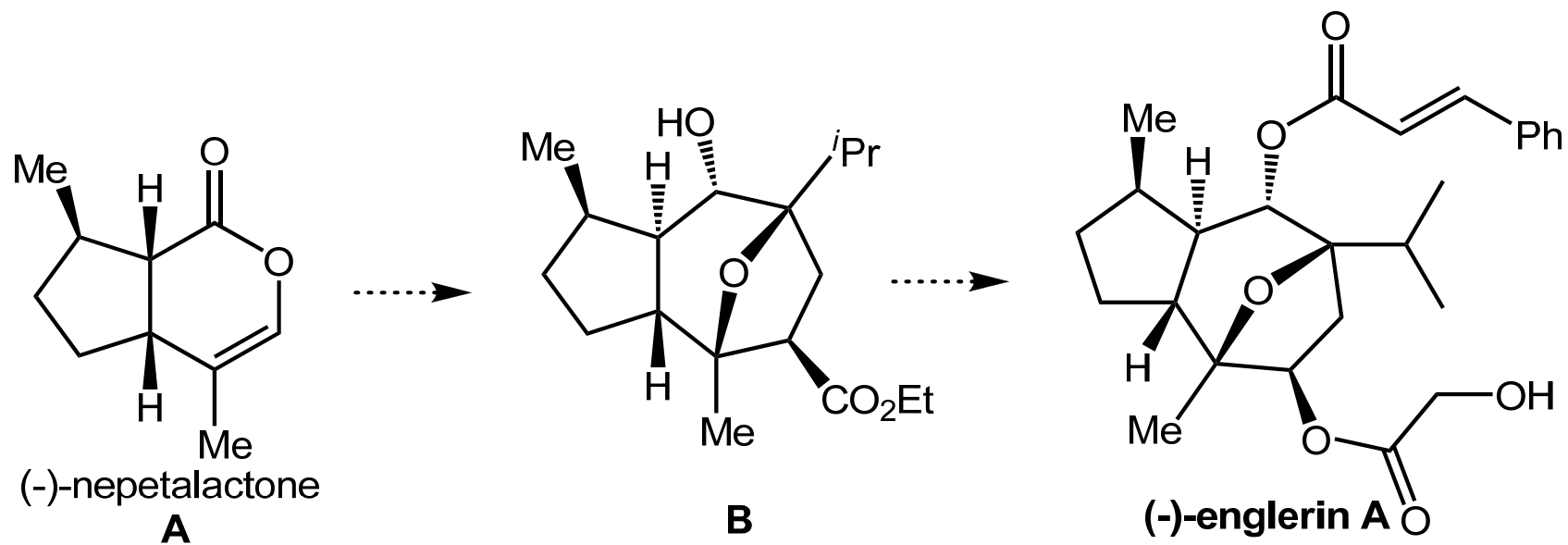


Mathias Christmann* *et al.* *Angew. Chem. Int. Ed.* **2009**, *48*, 9105–9108.

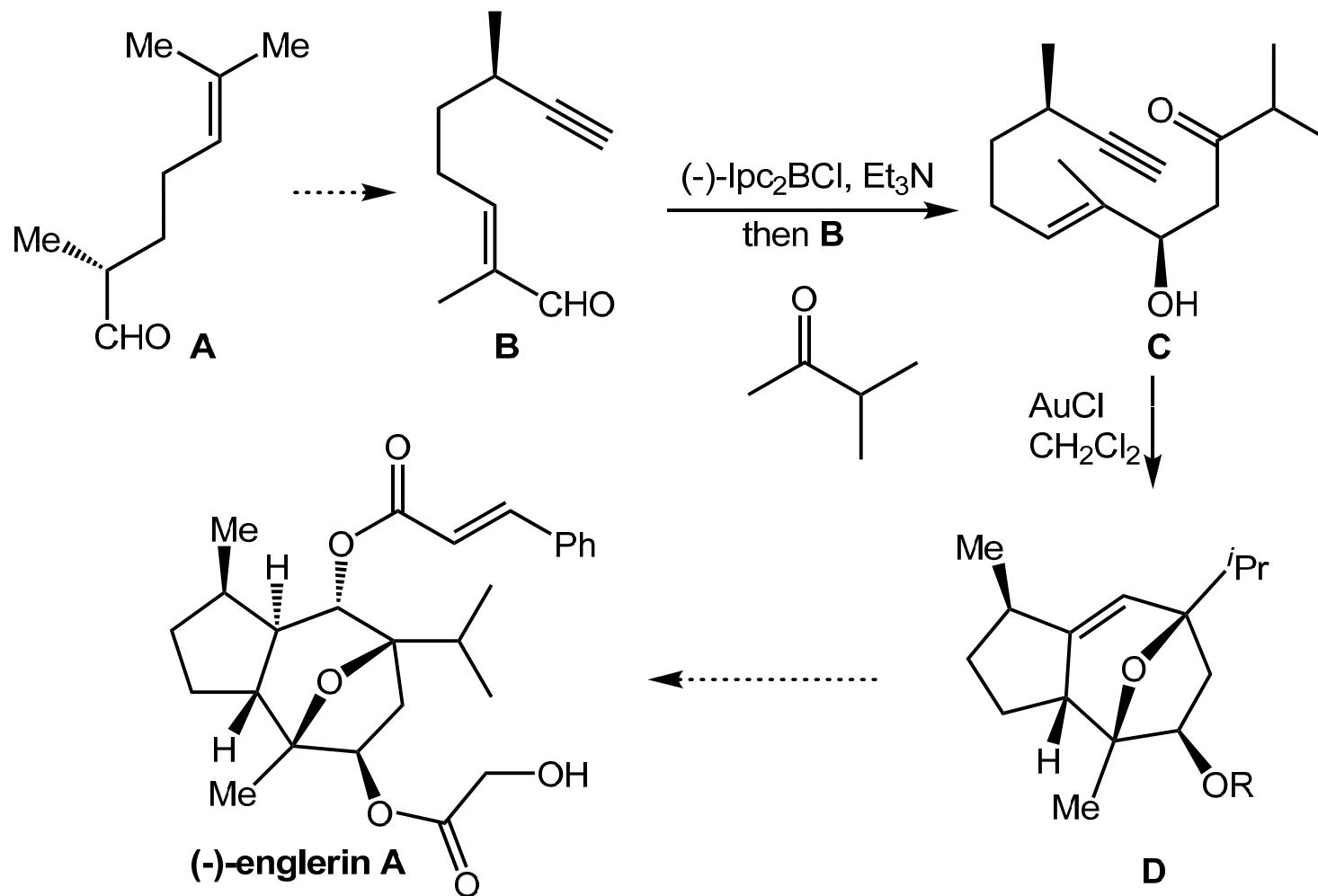


- 1、**Barbier** 反应，关环复分解反应，分子内跨环环氧开环反应
- 2、**15 steps, 11% overall yields**

Mathias Christmann* *et al.* *Angew. Chem. Int. Ed.* **2009**, 48, 9105–9108.

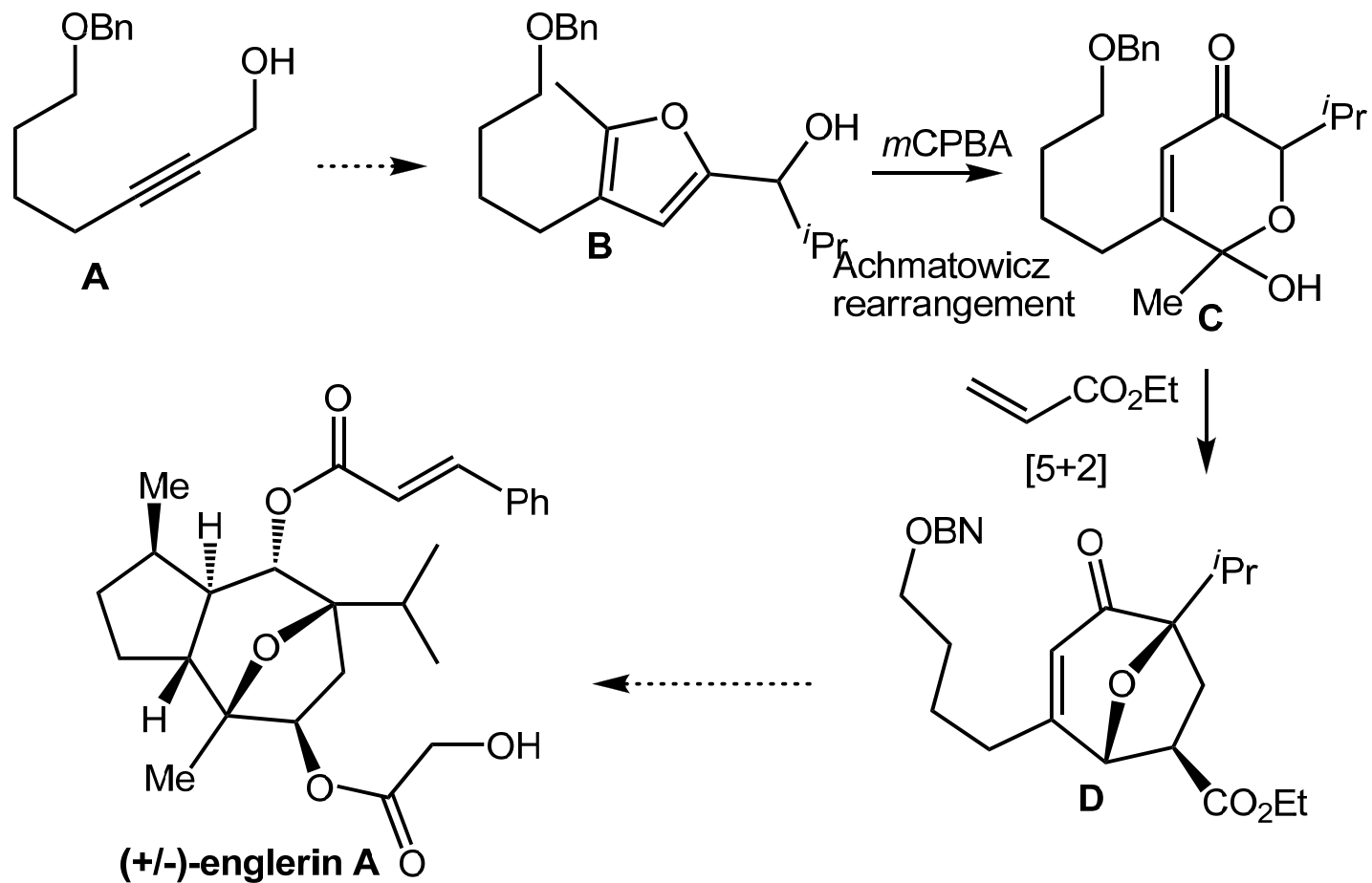


Mathias Christmann* *et al.* *Angew. Chem. Int. Ed.* **2011**, 55, 3998–4002.



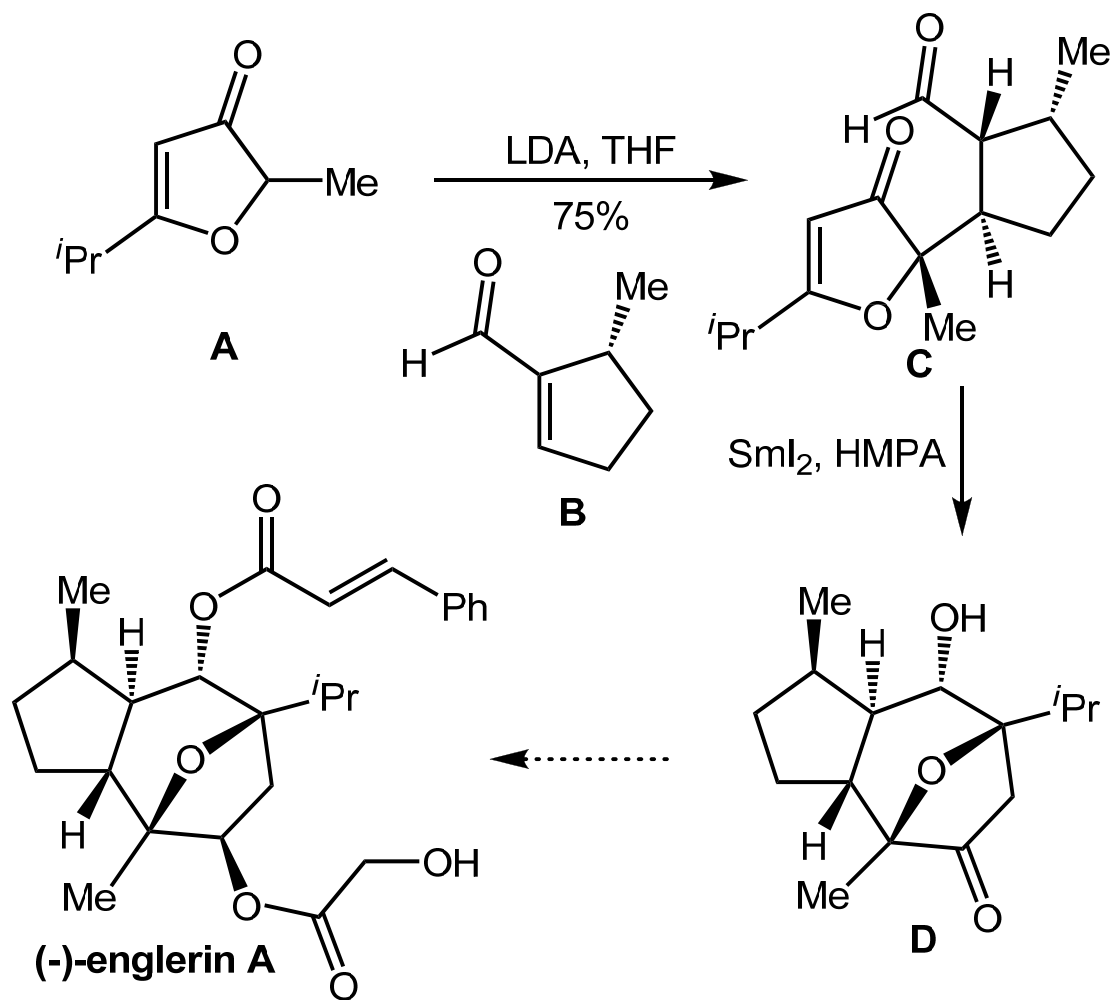
- 1、手性硼试剂催化的Aldol 反应，金催化的[2+2+2]环加成反应
- 2、15 steps, 8.1% overall yields
- 3、Protecting-Group Free

Dawei Ma* *et al.* *Angew. Chem. Int. Ed.* **2010**, 49, 3513–3516.



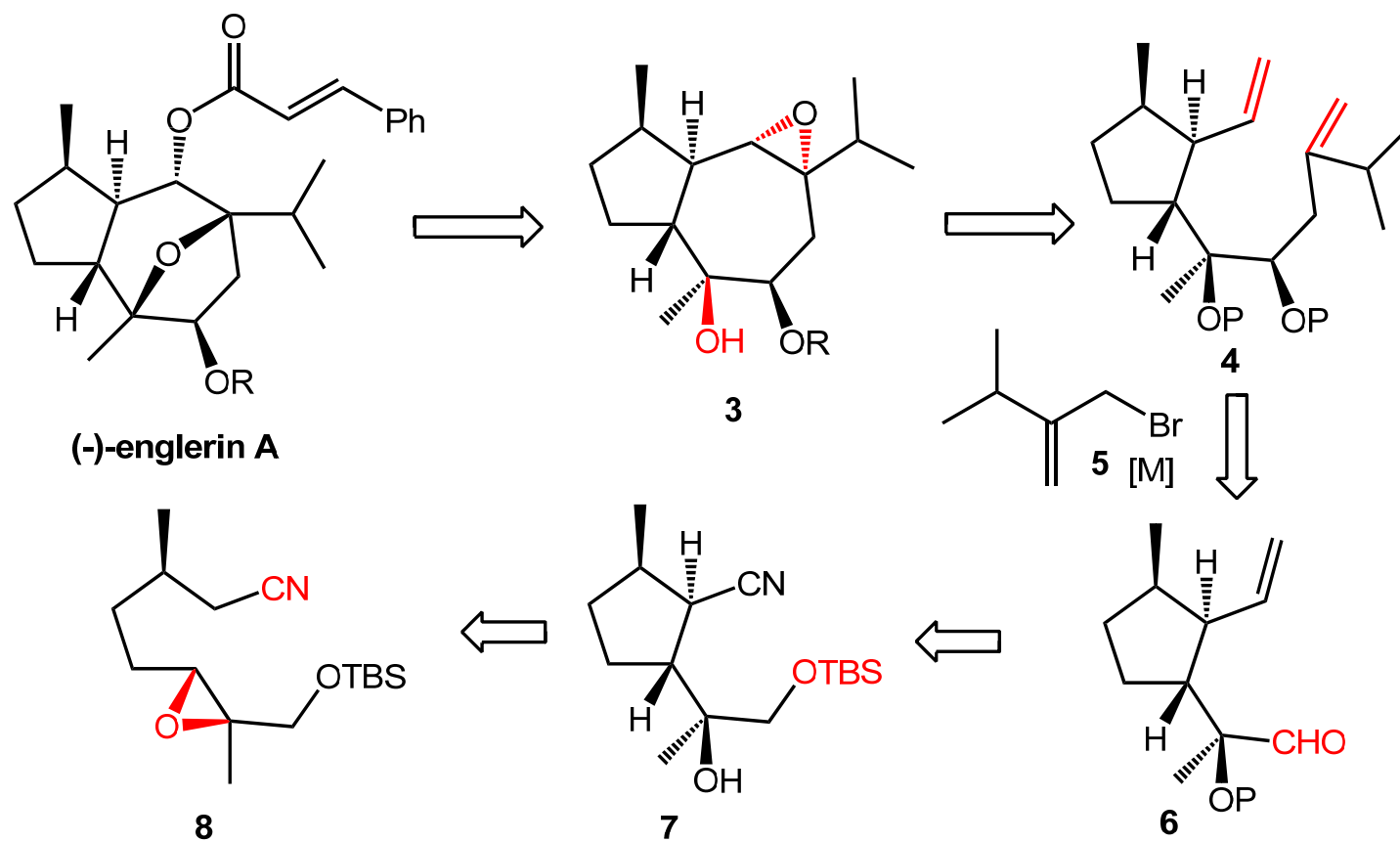
- 1、Achmatowicz rearrangement反应, [5+2]环加成反应
- 2、26 steps (消旋体)

K. C. Nicolaou*/David Y.-K. Chen* *et al.* *J. Am. Chem. Soc.* **2010**, 132, 8219–8222.

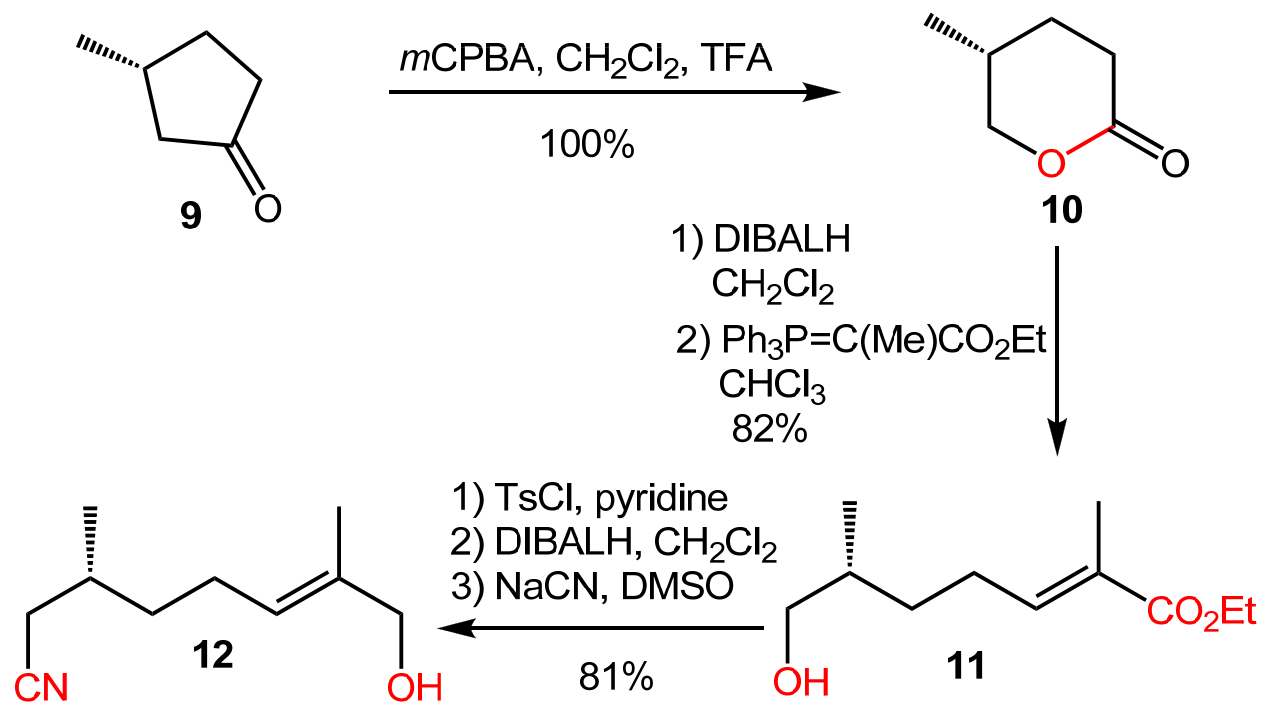


- 1、Michael反应, SmI_2 促进的还原偶联反应
- 2、8 steps, 20% overall yields

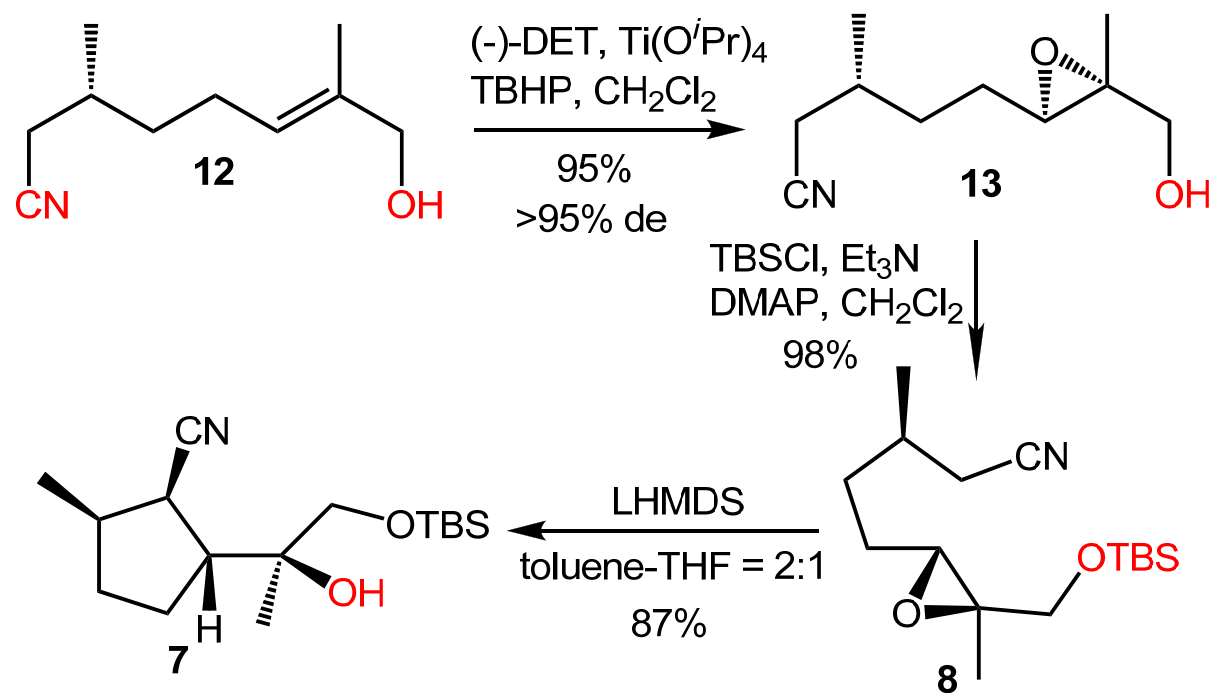
William J. Chain* *et al.* *J. Am. Chem. Soc.* **2011**, 133, 6553–6556.



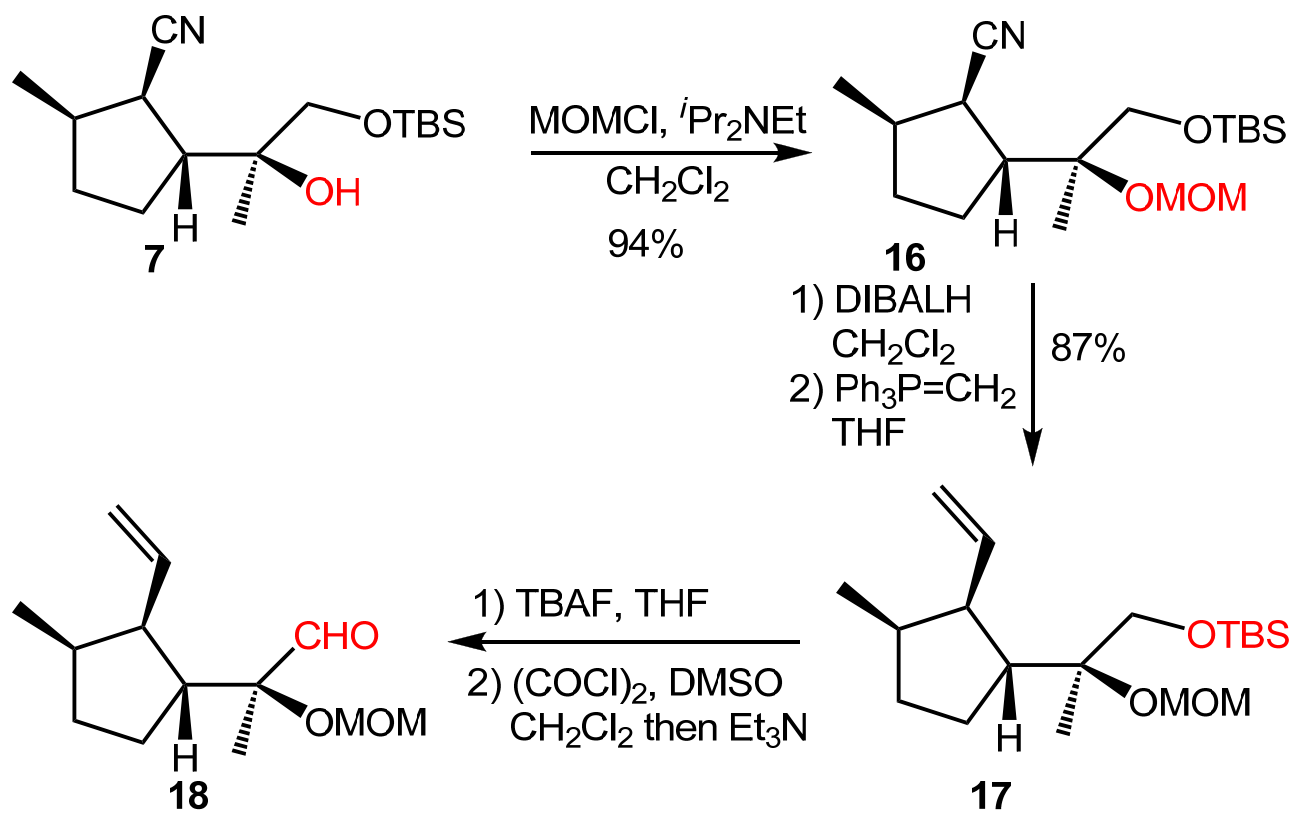
Susumi Hatakeyama* *et al.* *J. Org. Chem.* **2012**, *77*, 7364–7370.



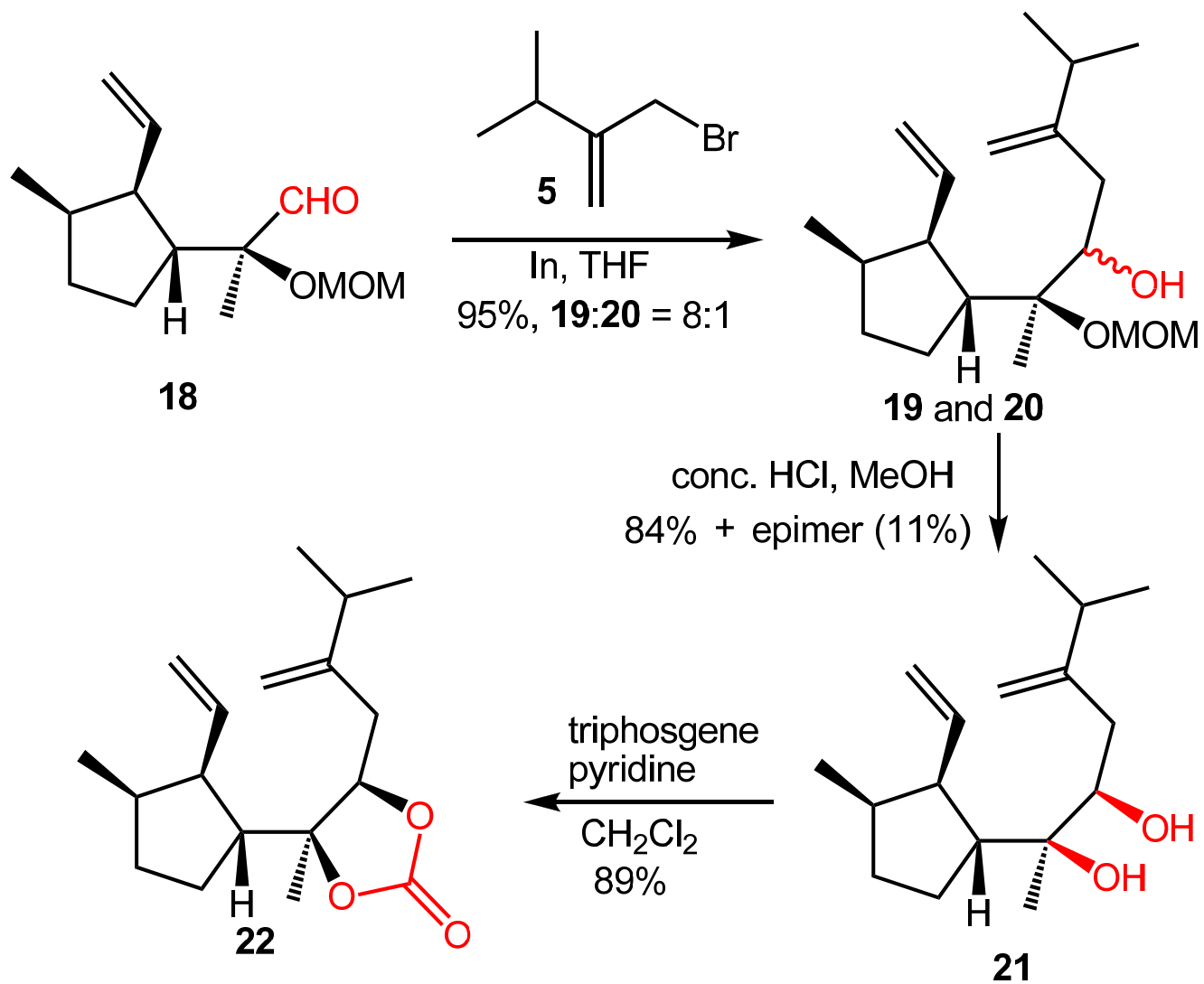
Susumi Hatakeyama* *et al.* *J. Org. Chem.* **2012**, *77*, 7364–7370.



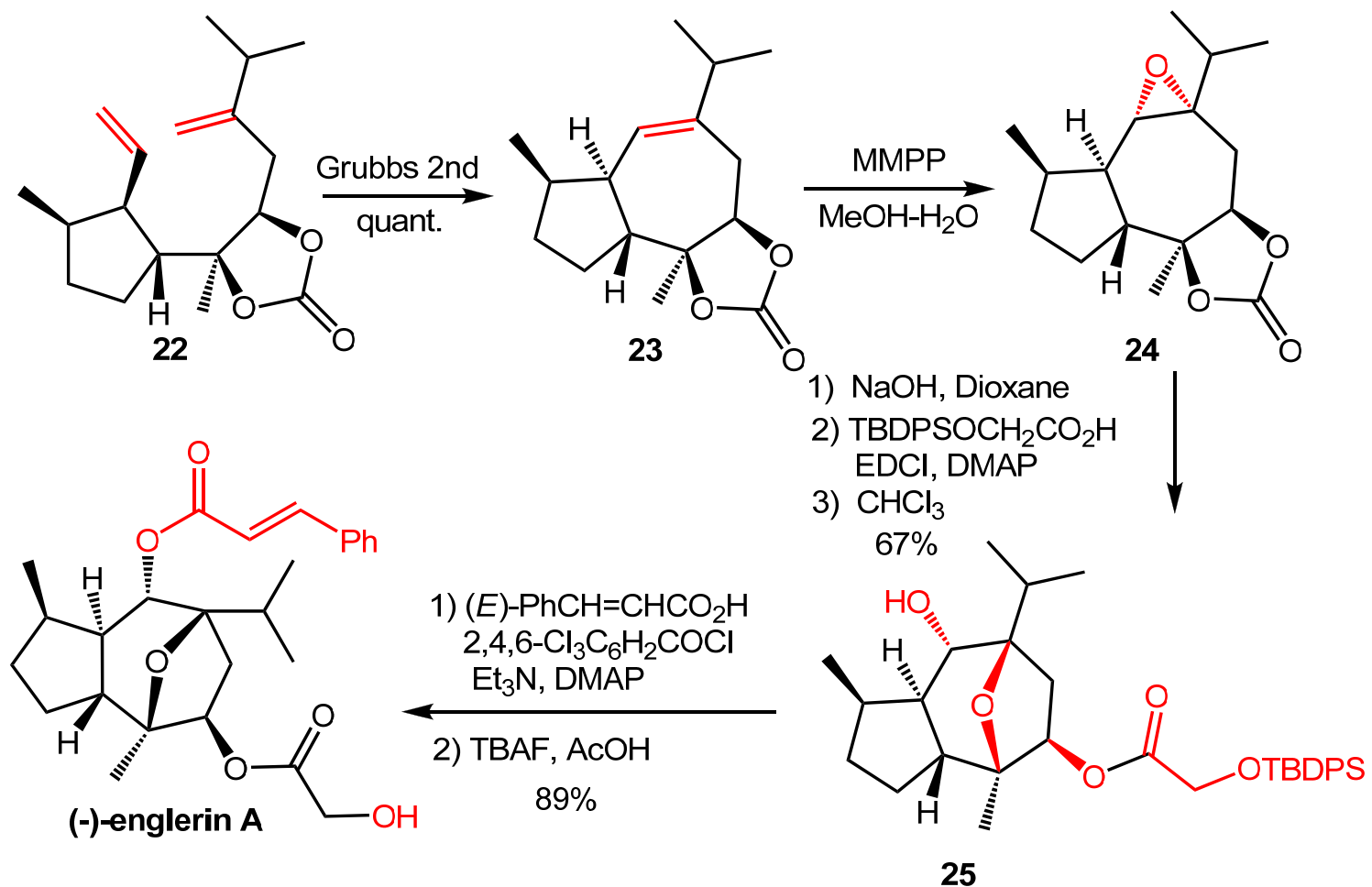
Susumi Hatakeyama* *et al.* *J. Org. Chem.* **2012**, *77*, 7364–7370.



Susumi Hatakeyama* *et al.* *J. Org. Chem.* **2012**, *77*, 7364–7370.



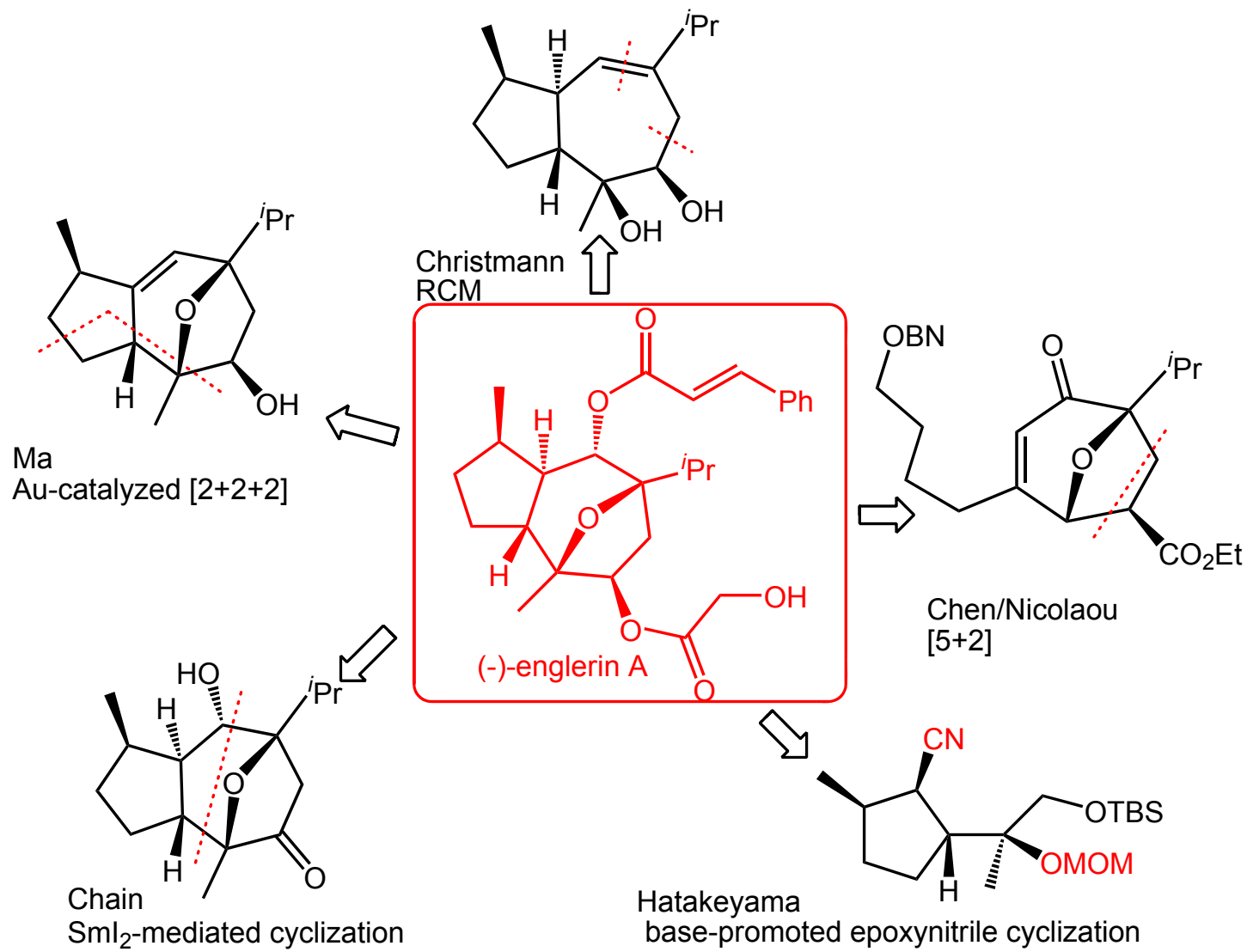
Susumi Hatakeyama* *et al.* *J. Org. Chem.* **2012**, *77*, 7364–7370.



- 1、 base promoted epoxynitrile cyclization
- 2、 24 steps, 14% overall yields

Susumi Hatakeyama* *et al.* *J. Org. Chem.* **2012**, *77*, 7364–7370.

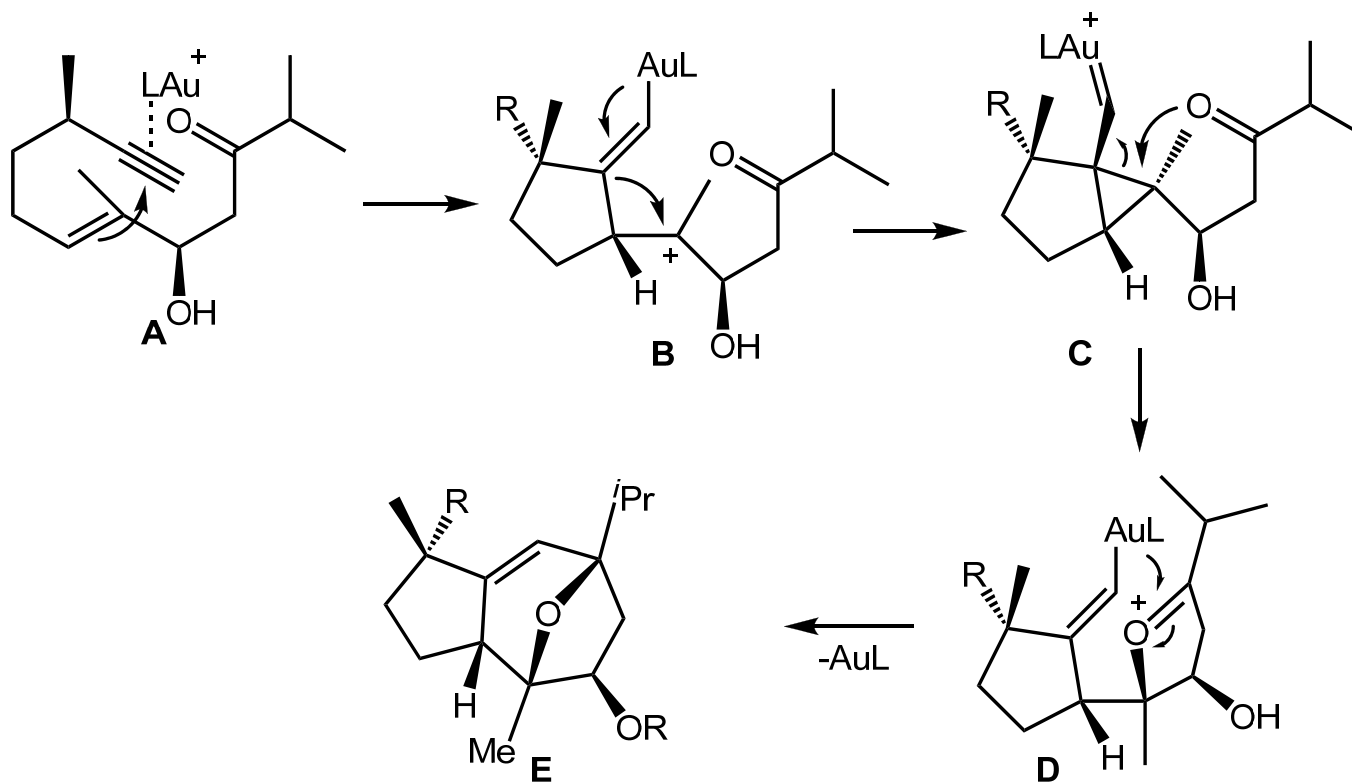
总结:



Englerin A (1) is a guaianes sesquiterpene that was isolated by Beutler and co-workers from the stem bark of *Phyllanthus engleri*, a plant indigenous to the East African countries of Tanzania and Zimbabwe. In a NCI 60-cell panel screening, this compound was found to be a potent and selective inhibitor of renal cancer cell lines at low nanomolar levels, while englerin B (2), lacking the C9 glycolate ester, was shown to be inactive.

We have accomplished the total synthesis of (-)-englerin A (1) from **9** in good overall yield (14%, 24 steps), which is highly stereoselective and applicable to the synthesis of various analogues with variations in not only ester groups but C4 and C7 substituents. In addition, the present work newly demonstrates the synthetic utility of Stork's epoxynitrile cyclization for the synthesis of highly substituted cyclopentanes.

Au-catalyzed [2+2+2] cyclization reaction



Swern oxidation

