文献报告

Total Synthesis of (±)-Merrilactone A

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检查人：段　英

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H. Zhai *et al.*
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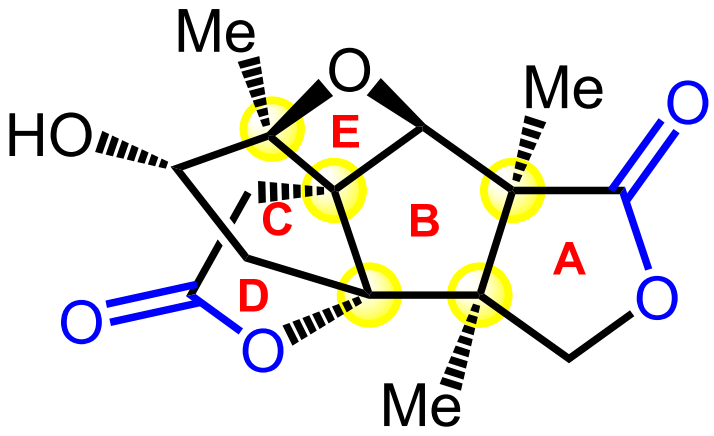
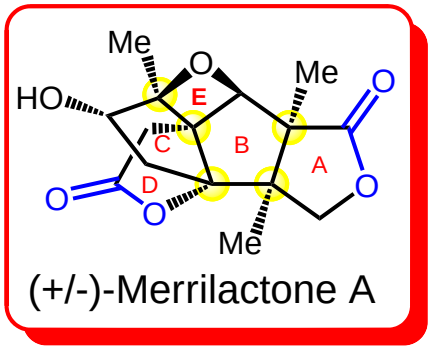
(±)-Merrilactone A

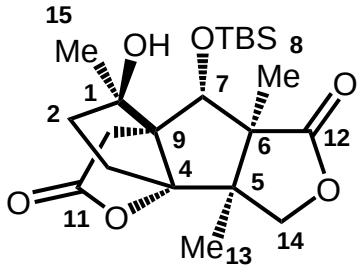


1. 倍半萜烯类化合物，2000年Fukuyama等从滇缅八角中分离得到。
2. 结构单元：五个并环、两个内酯、氧杂环丁烷、五个季碳中心。
3. 在胎鼠的皮质神经元研究中发现，该类化合物是一类促进神经突自然生长的非肽因子。
4. 目前已有五个课题组完成该化合物的全合成或形式全合成。

Retrosynthetic Analysis

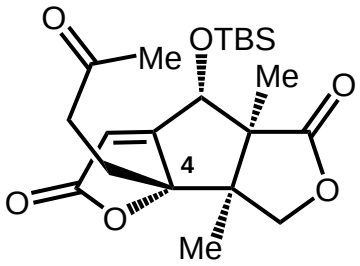


(+/-)-Merrilactone A



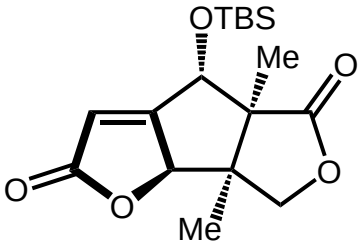
2

reductive carbonyl-alkene coupling



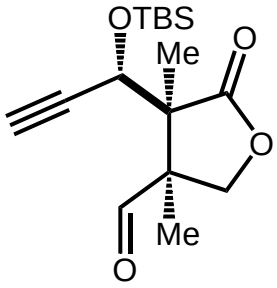
3

vinylogous Mukaiyama-Michael



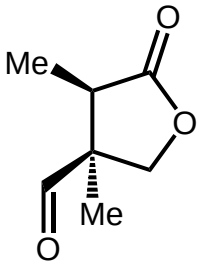
4

h-PKR



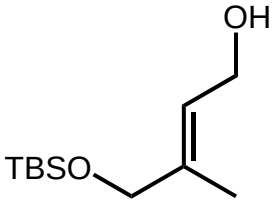
5

aldol reaction



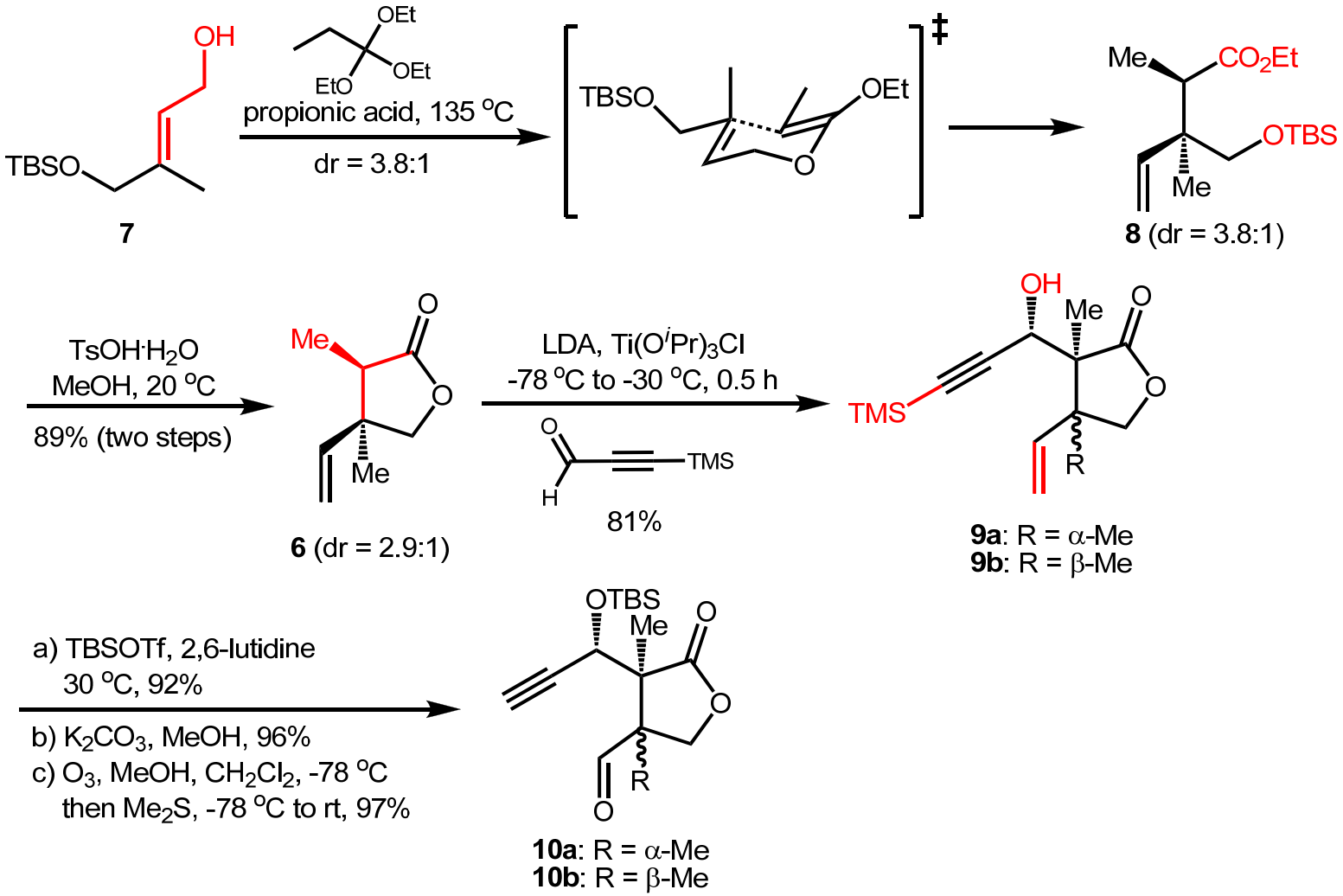
6

Johnson-Claisen rearrangement

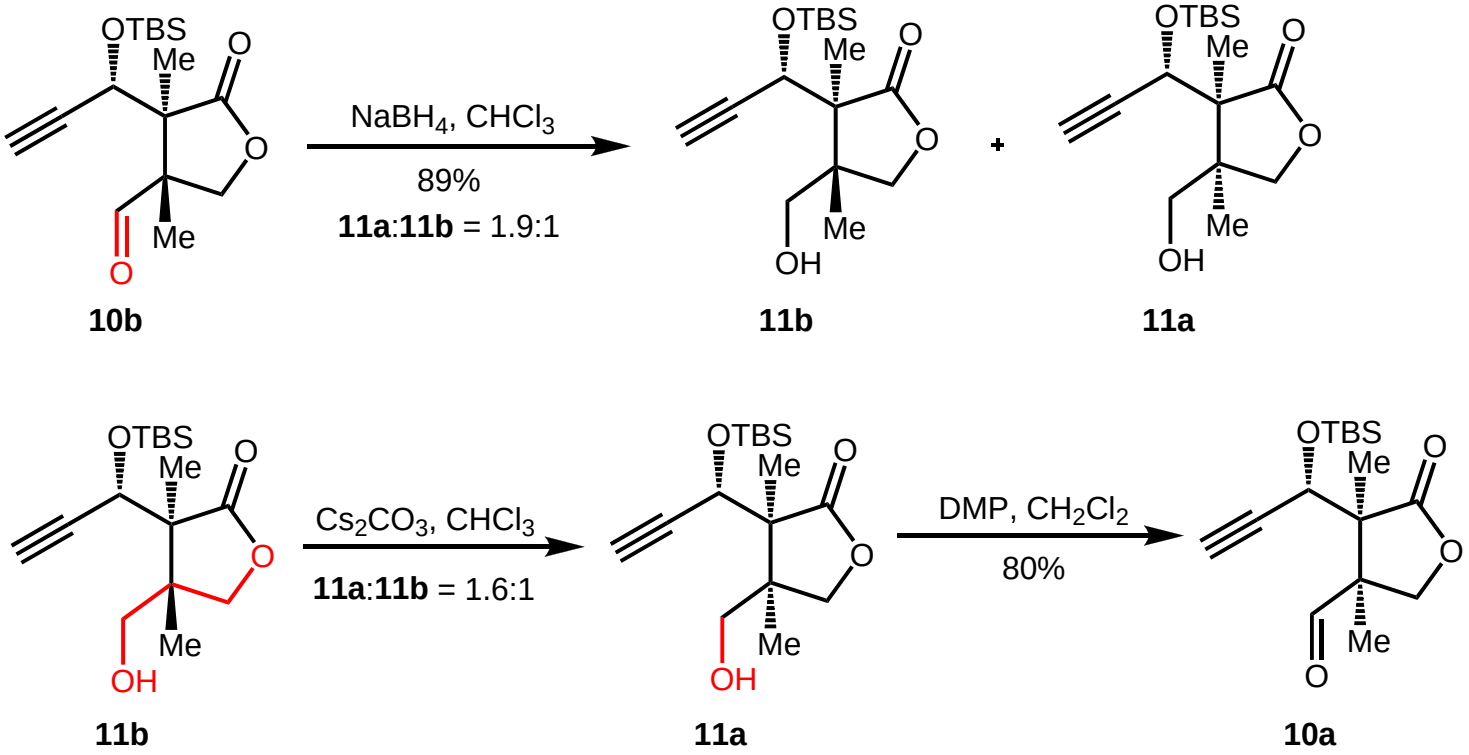


7

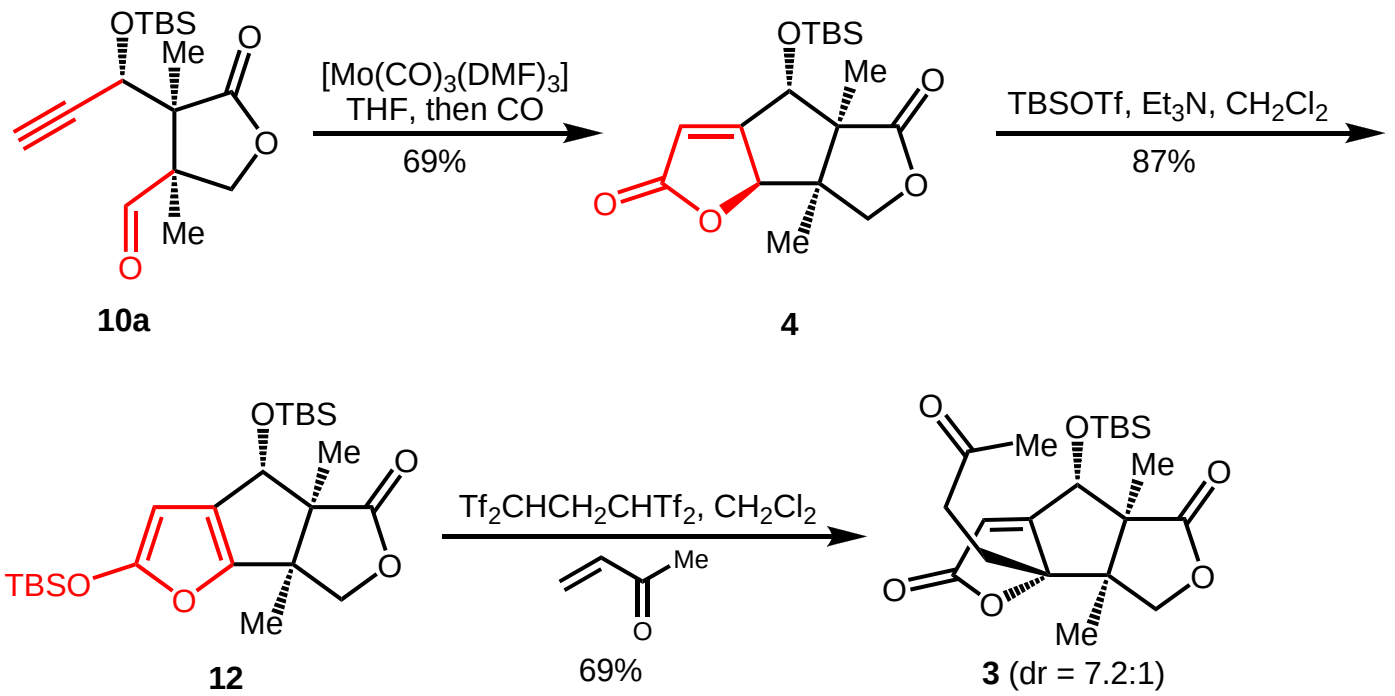
Synthesis of 10a



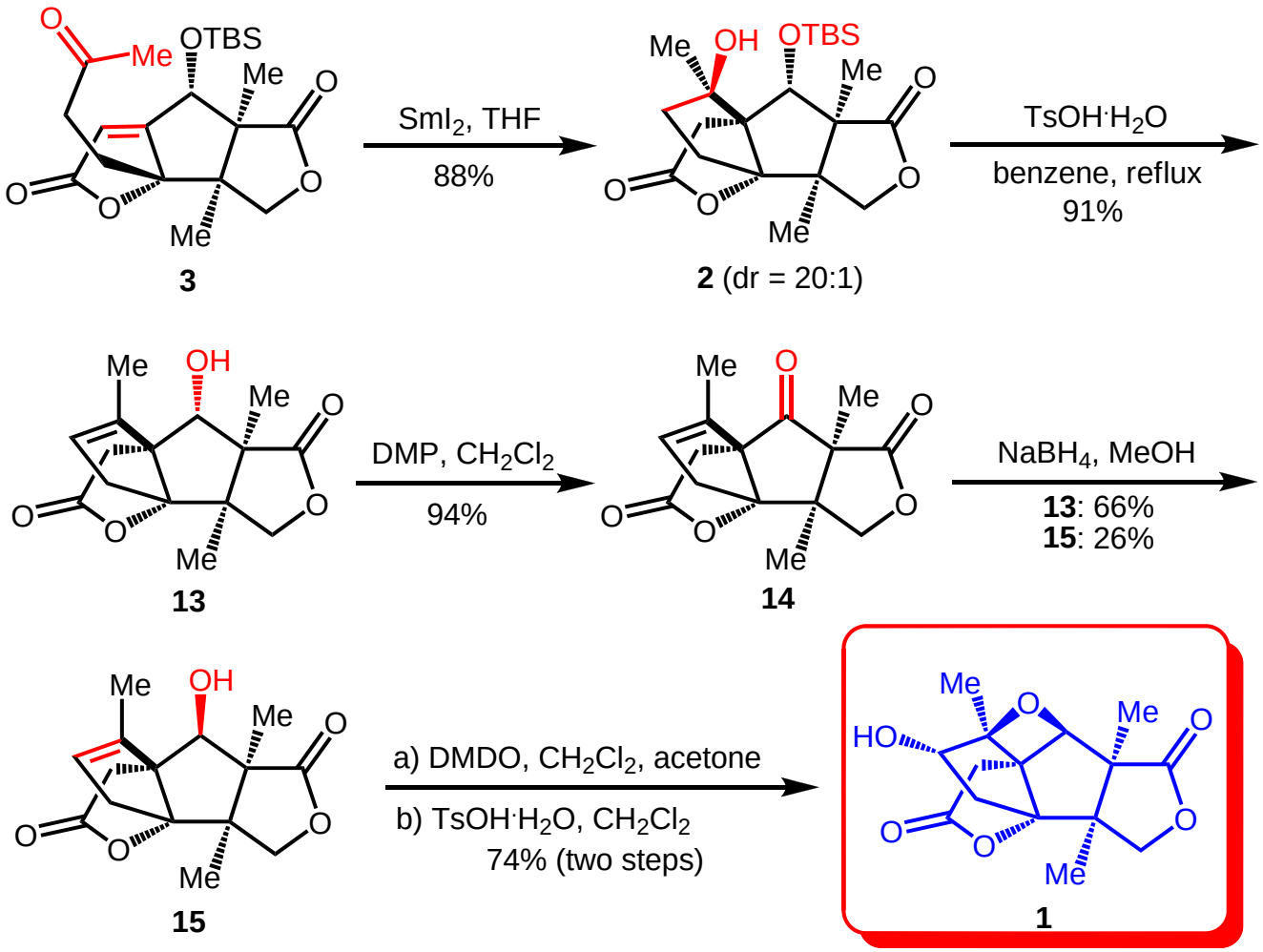
Synthesis of 10a



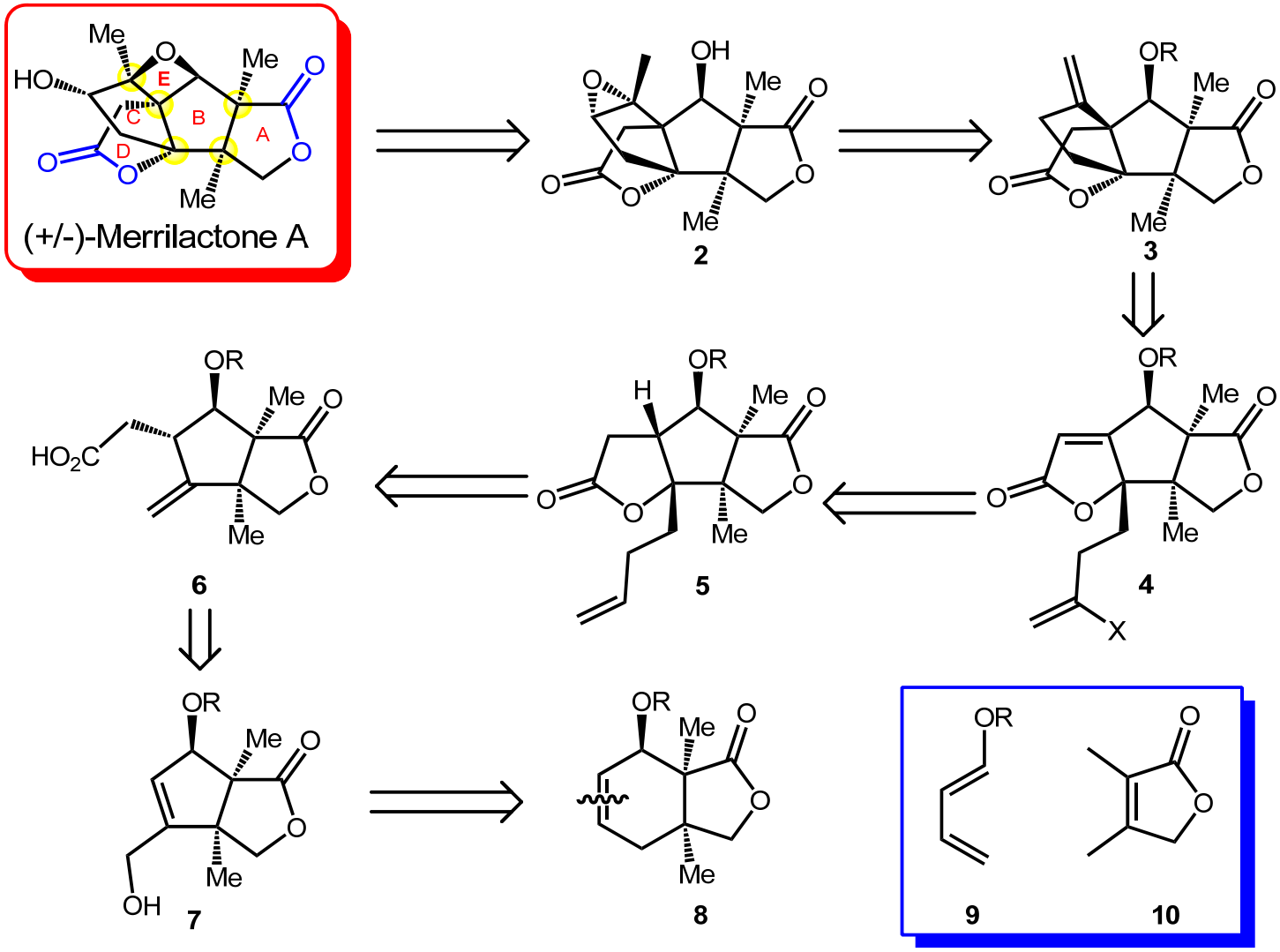
Synthesis of 3



Synthesis of (±)-Merrilactone A

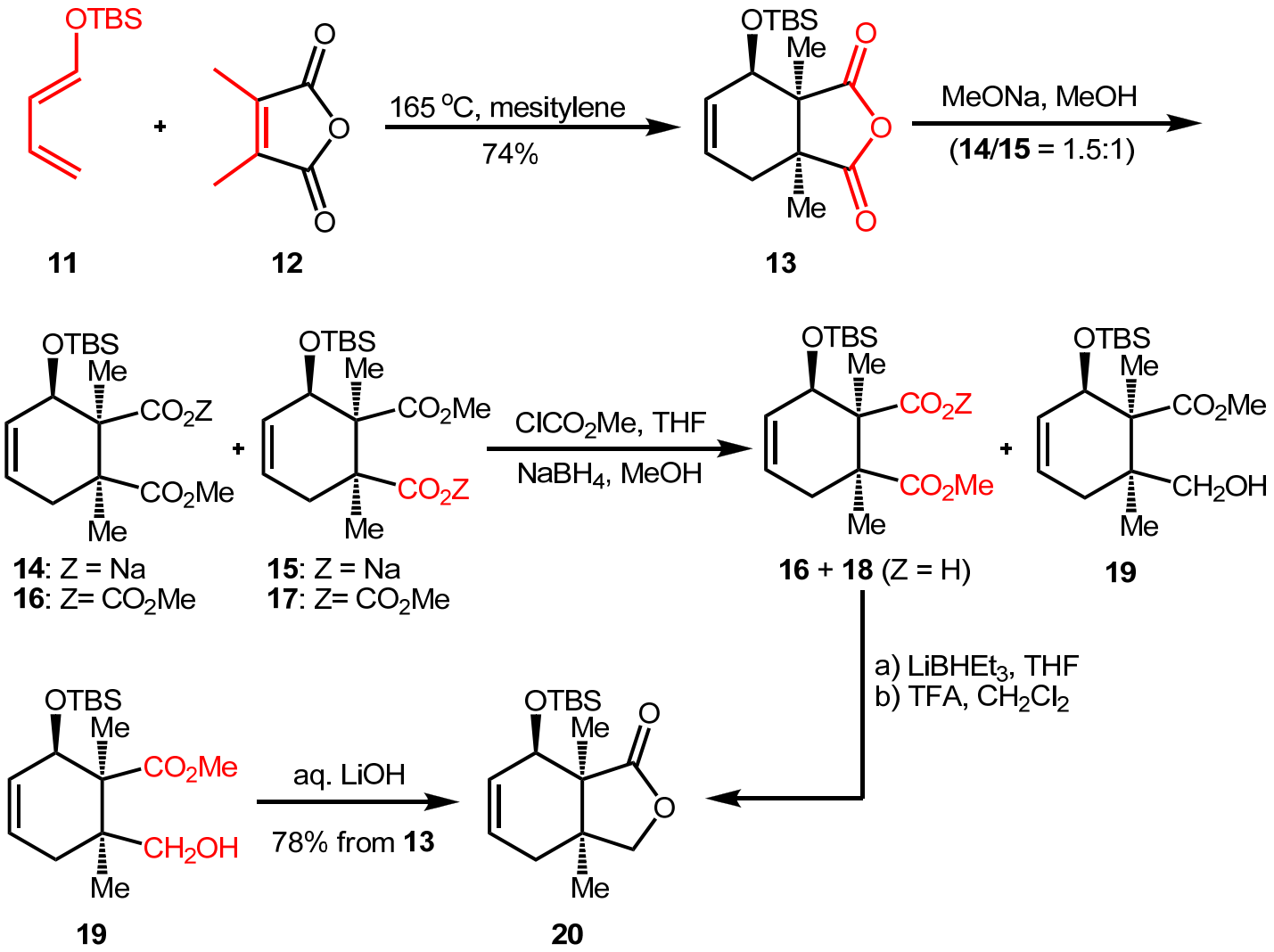


Retrosynthetic Analysis

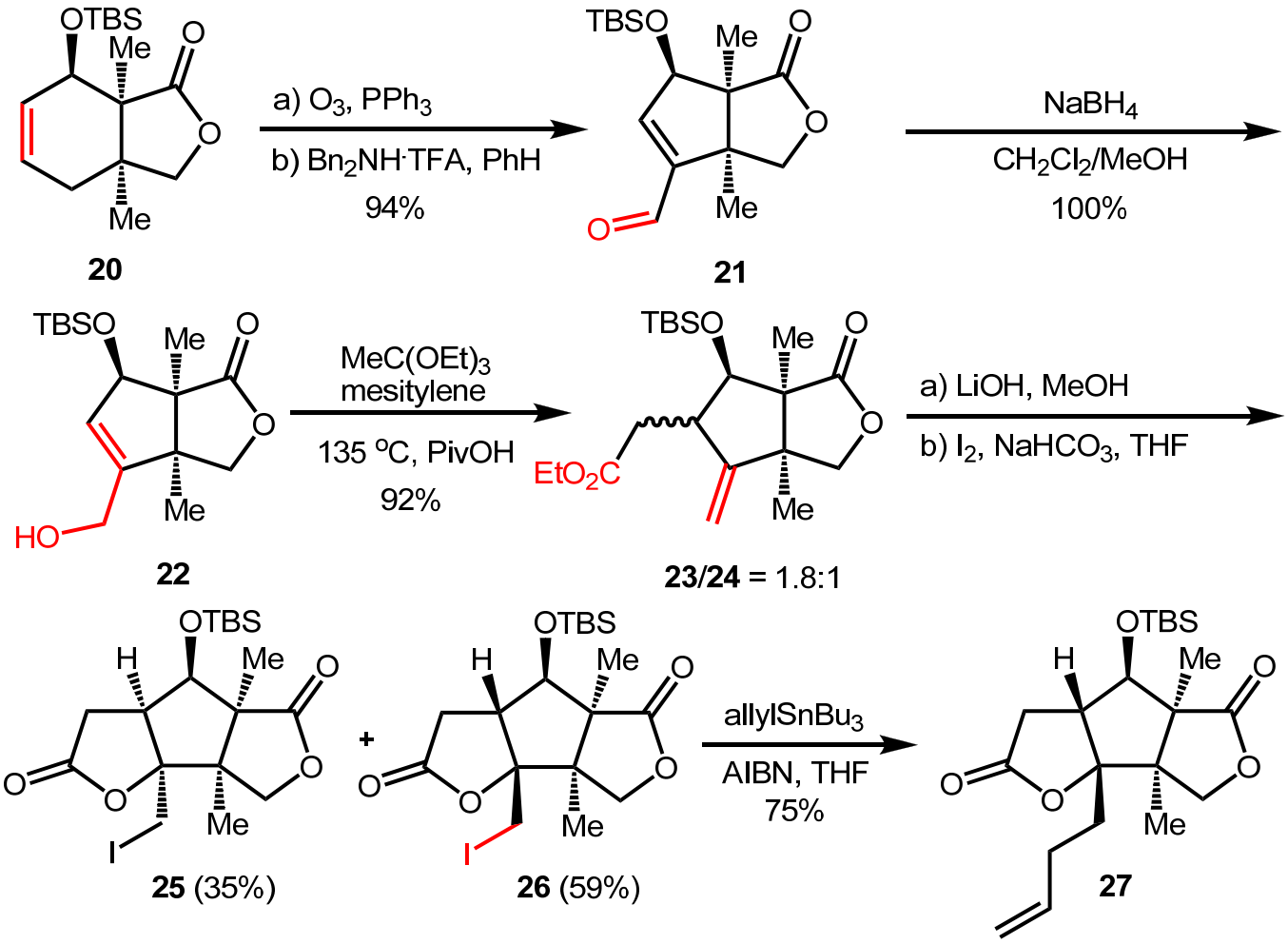


S. J. Danishefsky et al. *J. Am. Chem. Soc.* **2002**, *124*, 2080

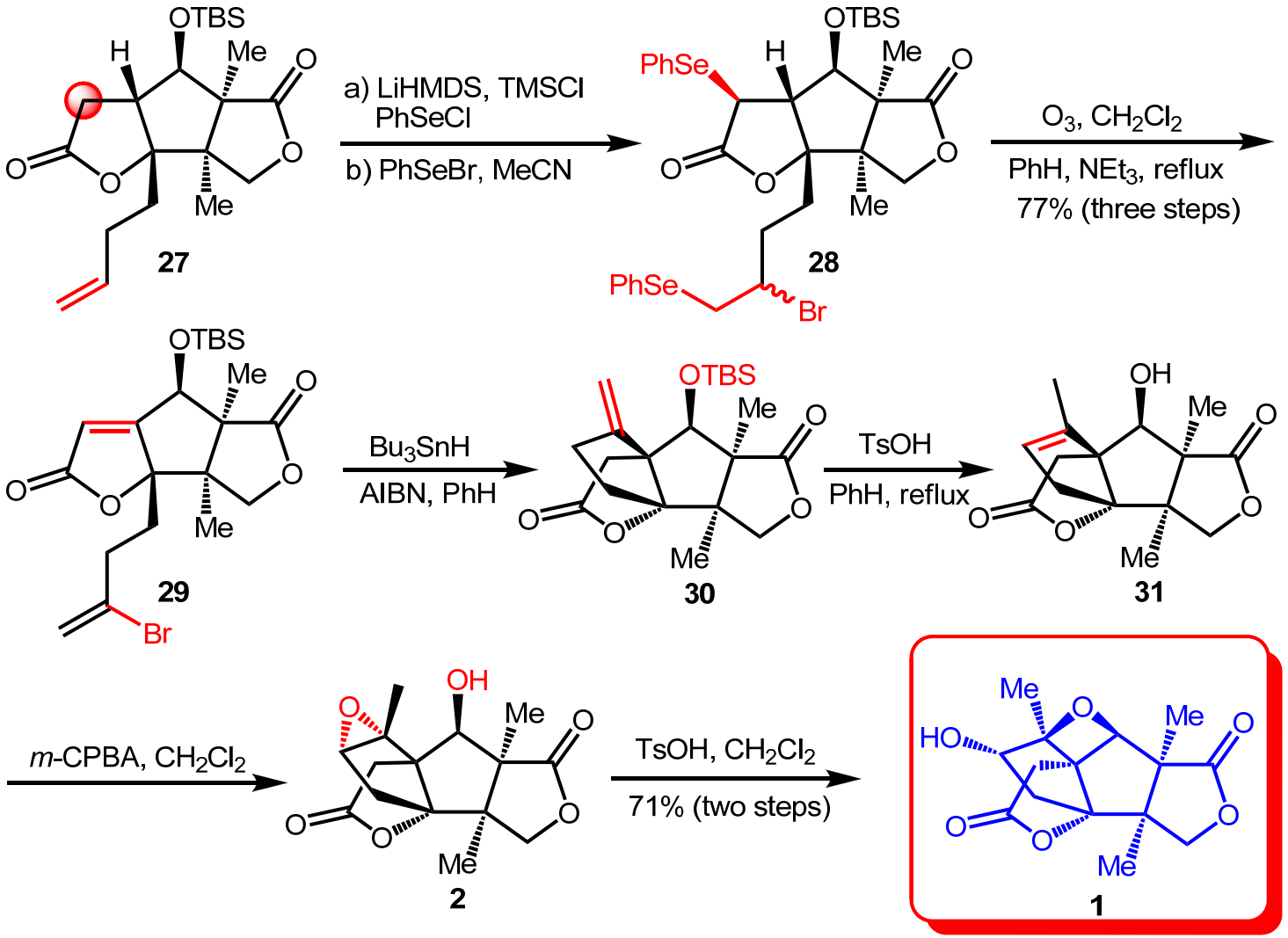
Synthesis of 20



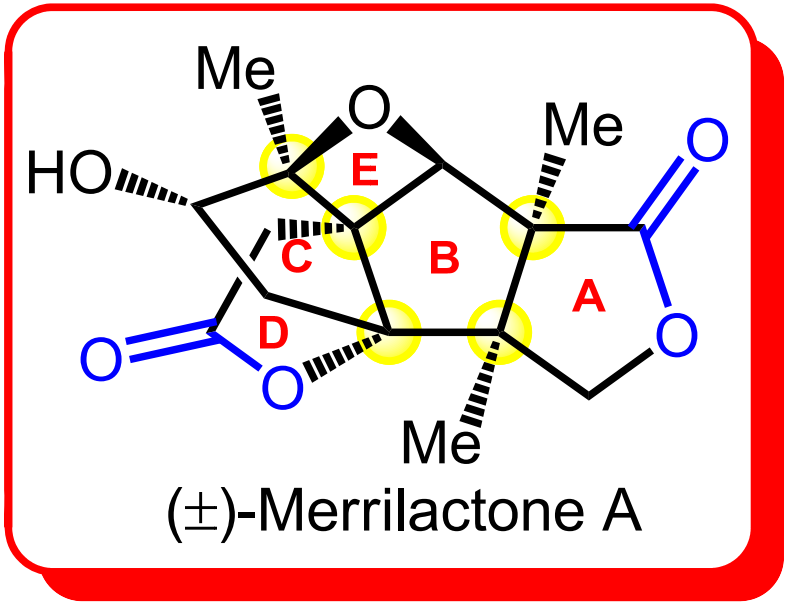
Synthesis of 27



Synthesis of (±)-Merrilactone A



Summary



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1. 15步
2. 主要涉及反应：
   Johnson–Claisen rearrangement
   hetero-Pauson–Khand reaction
   Mukaiyama-Michael reaction

S. J. Danishefsky *et al.*
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1. 20步
2. 主要涉及反应：
   D-A reaction
   Claisen rearrangement

Merrilactone **A**, a complex cage-shaped pentacyclic sesquiterpene, was isolated from pericarps of Illicium merrillianum by Fukuyama and co-workers in 2000. Its structure was established by NMR spectroscopic and X-ray crystallographic analyses, and the absolute configuration was determined by using the Mosher protocol. In addition to an oxetane moiety, two lactone functionalities, and a highly substituted cyclopentane ring at its core, this molecule contains seven contiguous chiral centers, including five quaternary ones. Moreover, this sesquiterpene was identified as a nonpeptidal neurotrophic factor that promoted neurite outgrowth in the culture of fetal rat cortical neurons. Owing to its unique structure as well as the potential officinal value for neurodegenerative diseases, merrilactone **A** has attracted considerable attention from the synthetic community. So far, Danishefsky, Inoue and Hirama, Mehta, Frontier, Greaney and their respective co-workers have accomplished its total or formal syntheses. Relevant synthetic studies have been documented for this natural product. Herein we wish to report a novel and efficient approach to the synthesis of (±)-**1**.

In summary, we have accomplished an efficient total synthesis of (±)-merrilactone **A** in fifteen reaction steps for the shortest sequence from **7**, which is a known compound. Key features of the current synthesis include: 1) Johnson-Claisen rearrangement and the subsequent deprotection–lactonization to generate the A ring, 2) intramolecular hetero-Pauson–Khand reaction to construct the B and D rings in one step, and 3) vinylogous Mukaiyama–Michael reaction and reductive carbonyl–alkene coupling to assemble the C ring.

谢谢！