

# Literature Report

## Total Synthesis of Bryostatin 3

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Checker: Xin-Wei Wang

June 23, 2020

Dalian Institute of Chemical Physics

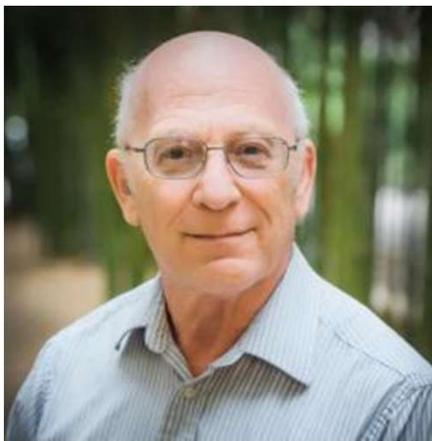


Trost, B. M.\*; Wang, Y. *et al.* *Science* **2020**, 368,1007.

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# CV of Prof. Myers, A. G.

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**Prof. Trost. B. M.**

**1958-1962 B.S. (University of Pennsylvania )**

**1962-1965 Ph.D. (MIT)**

**1965-1987 Prof. (University of Wisconsin)**

**1987-now Prof. (Stanford University)**

## **Research Fields:**

- ◆ Developing the tools, i.e., the reactions and reagents;
- ◆ Creating the proper network of reactions to make complex targets readily available from simple starting materials.

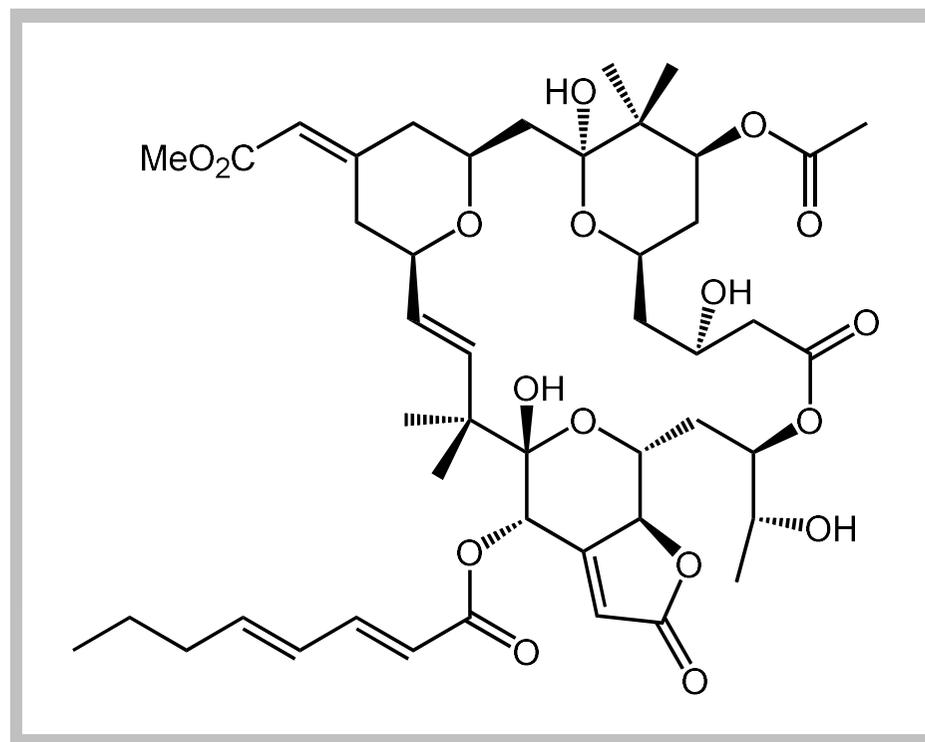
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- ◆ **Introduction**
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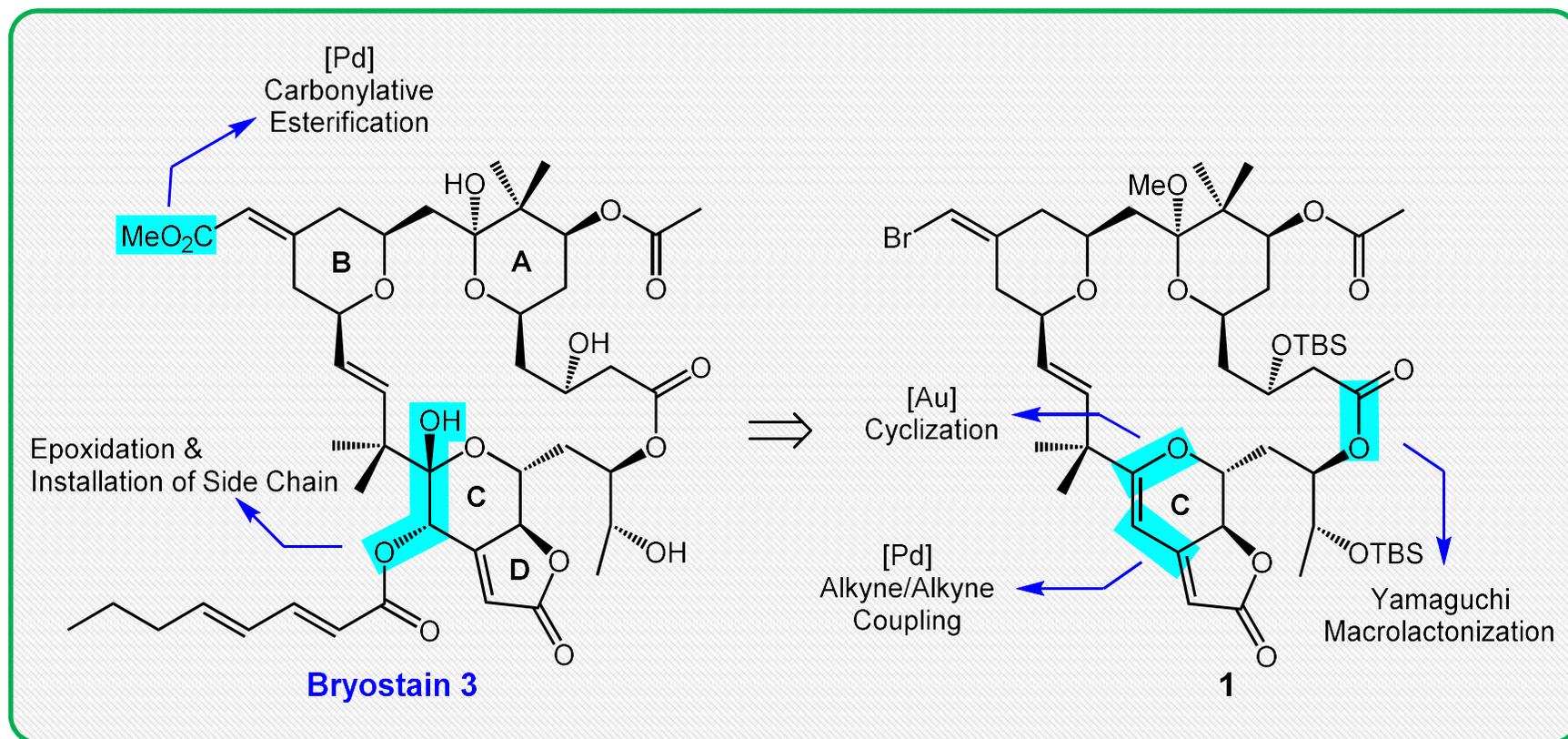
# Introduction-Bryostatin 3

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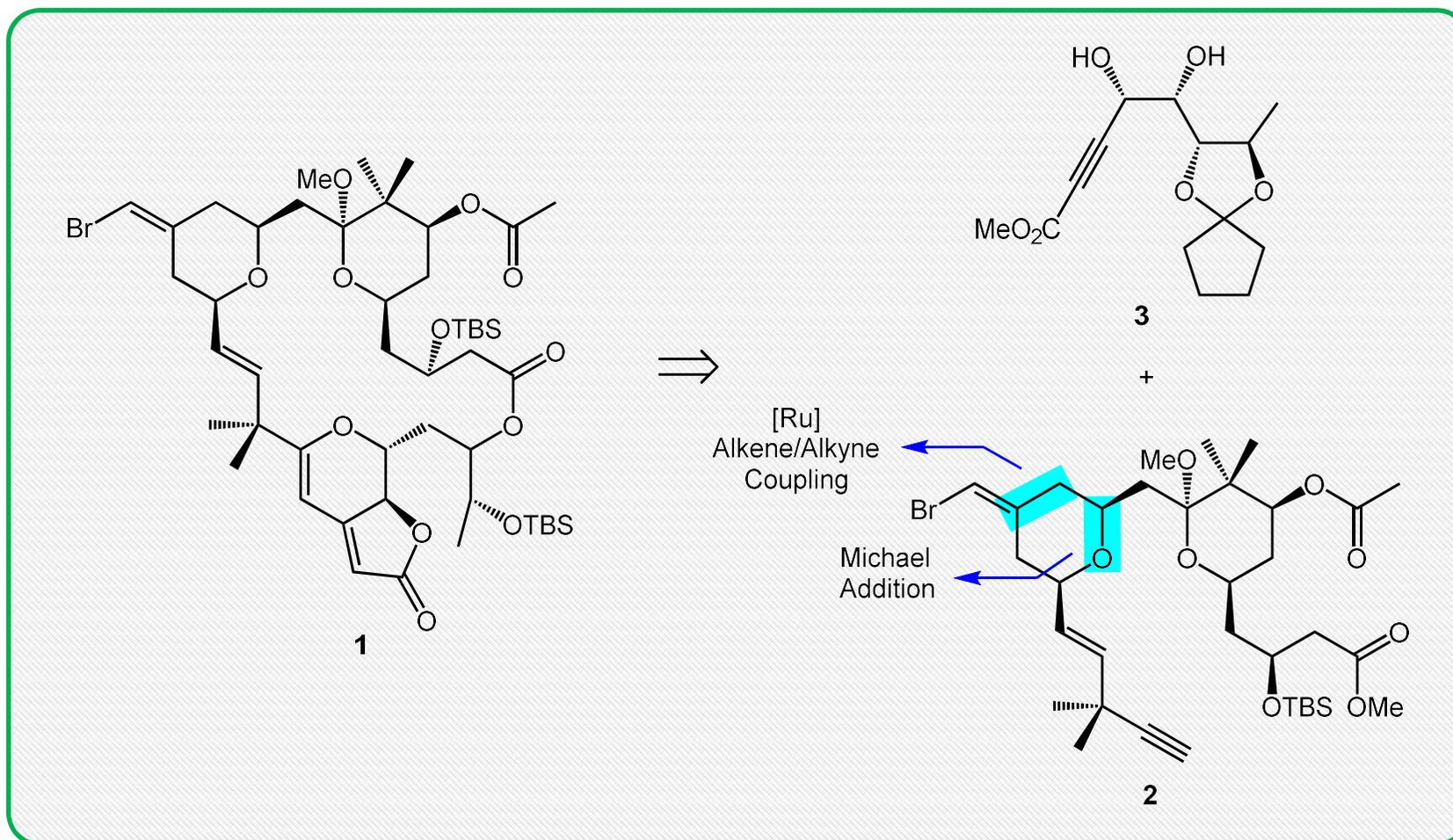


- ◆ Isolated from the marine bryozoan *Bugula neritina*
- ◆ Polycyclic structures
- ◆ A macrolide (26)

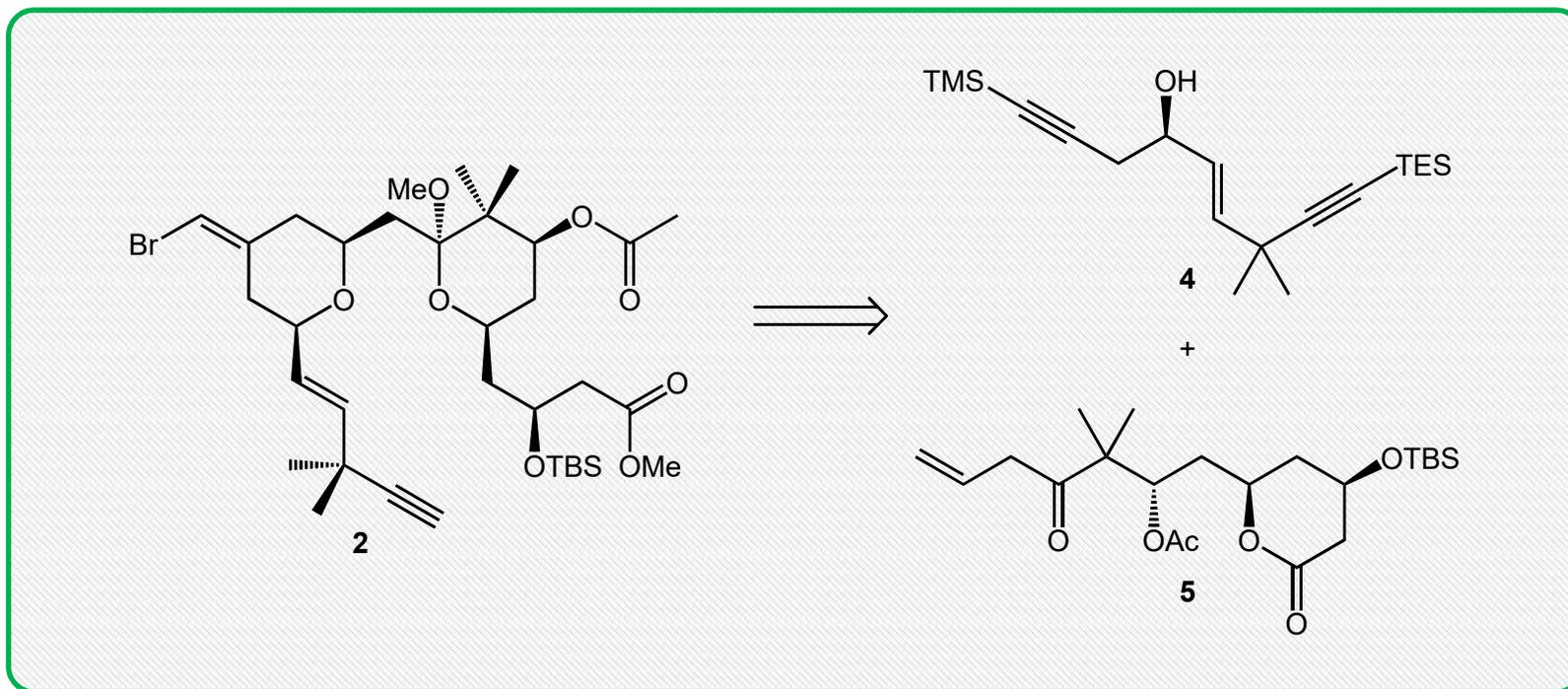
# Retrosynthetic Analysis



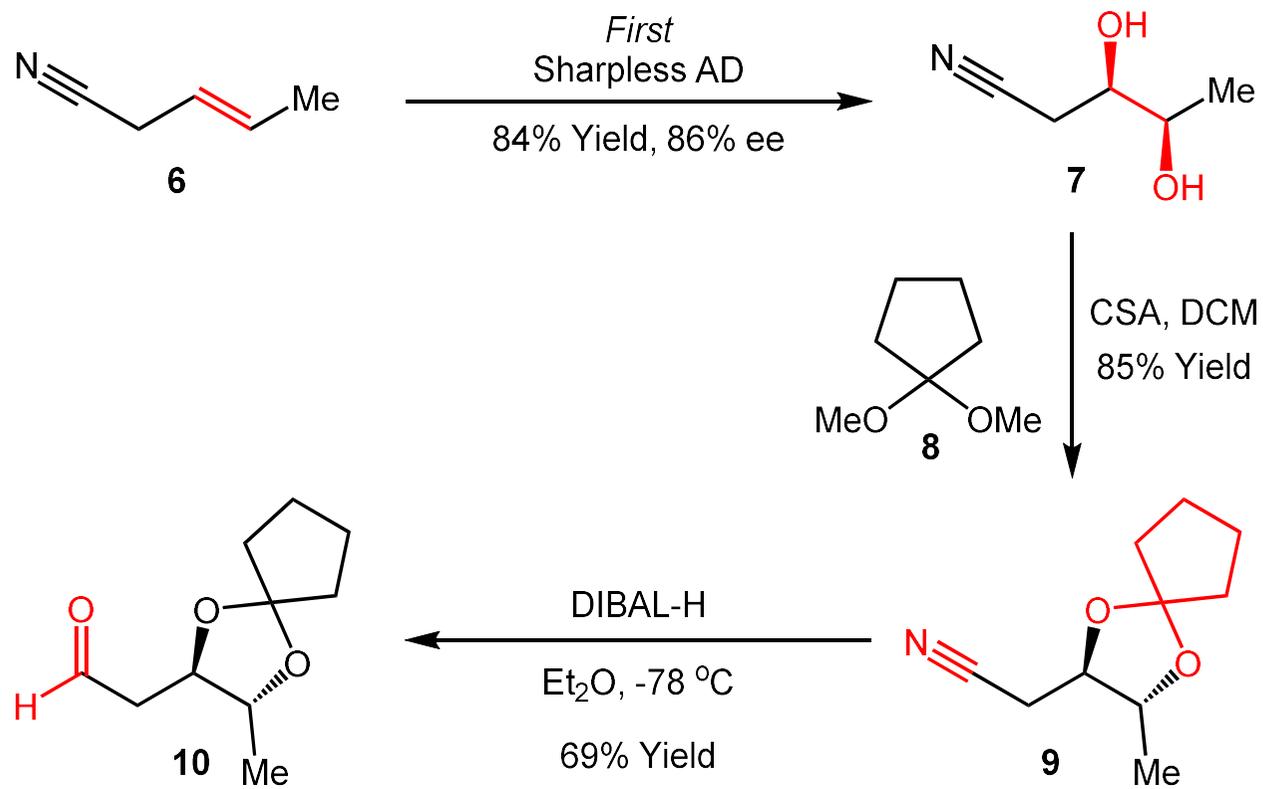
# Retrosynthetic Analysis



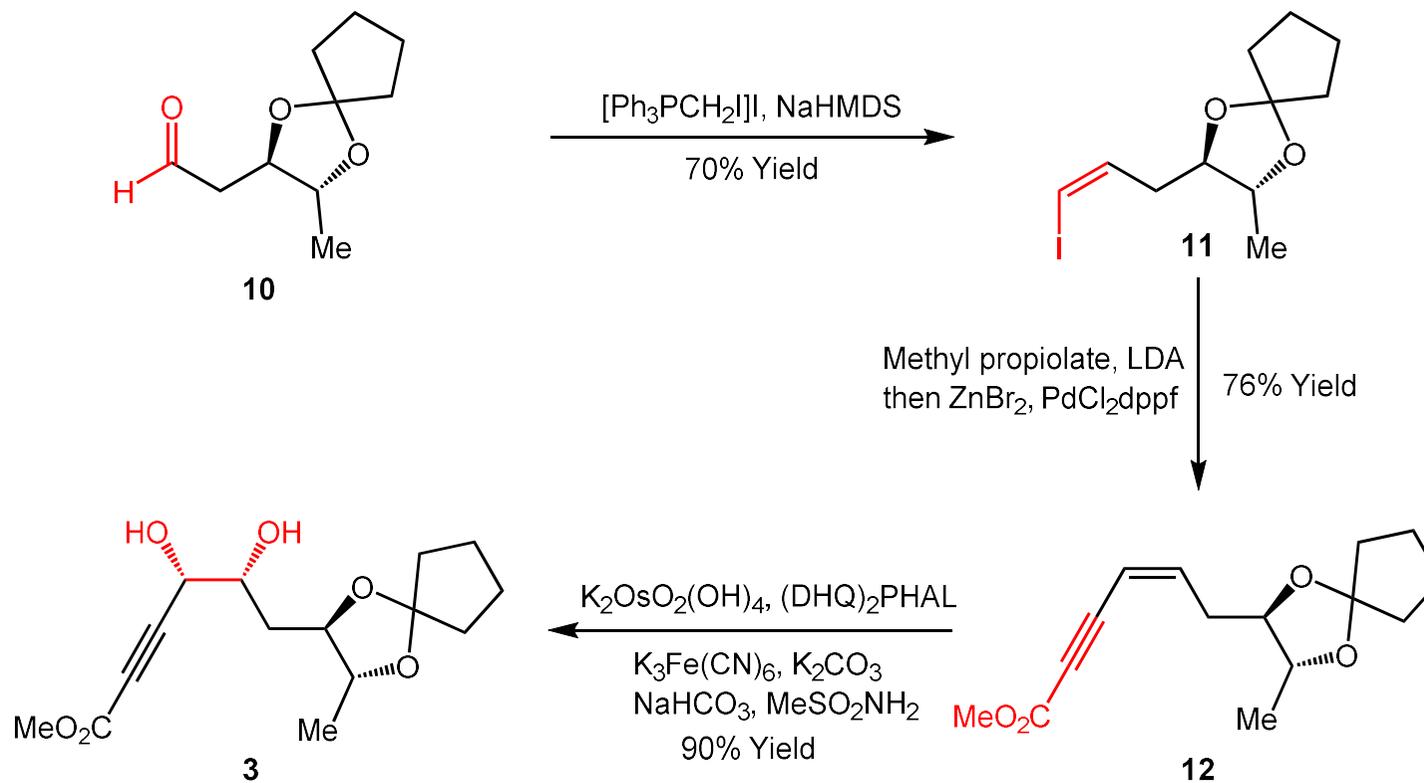
# Retrosynthetic Analysis



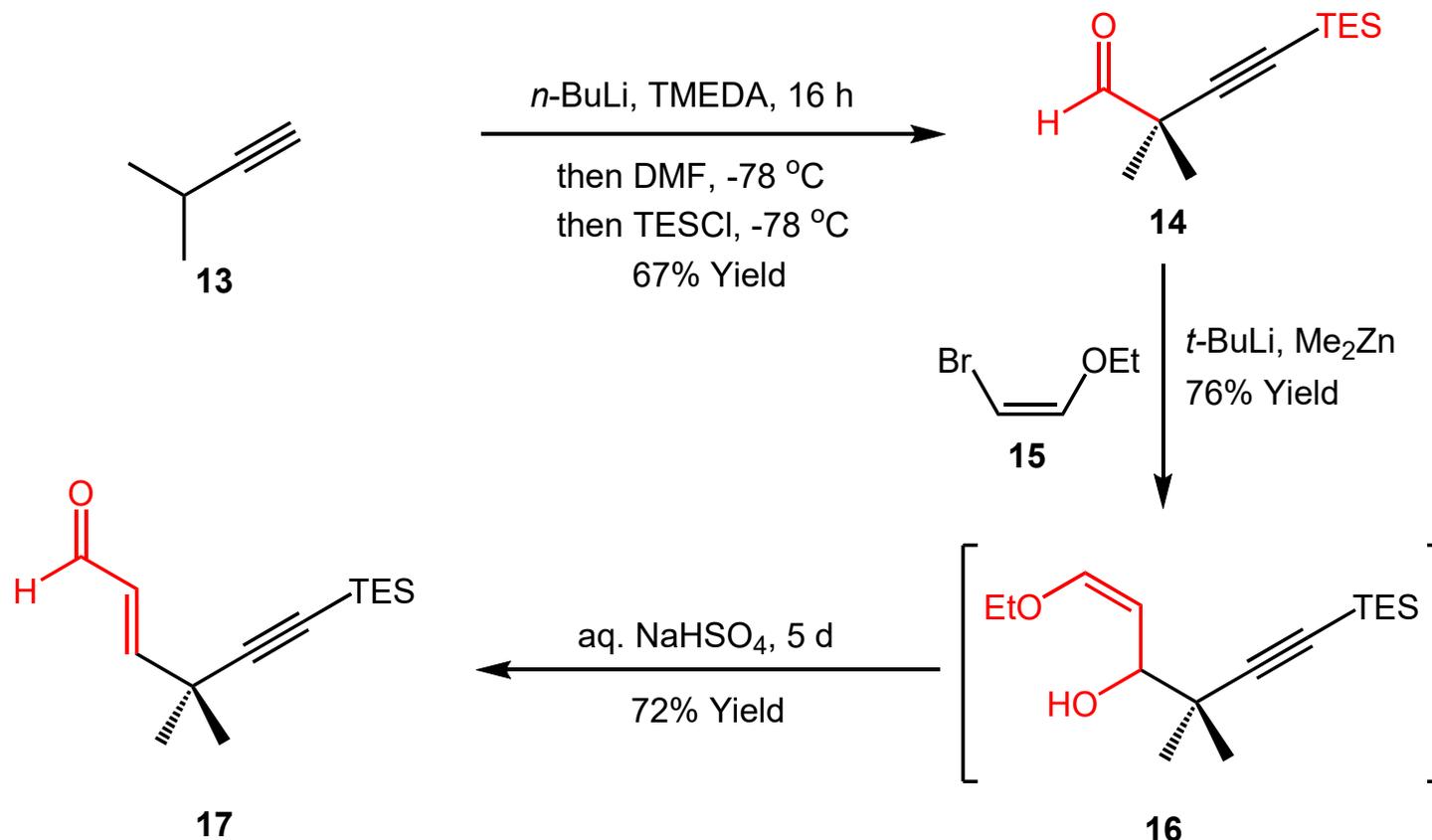
# Synthesis of Intermediate 10



# Synthesis of Intermediate 3

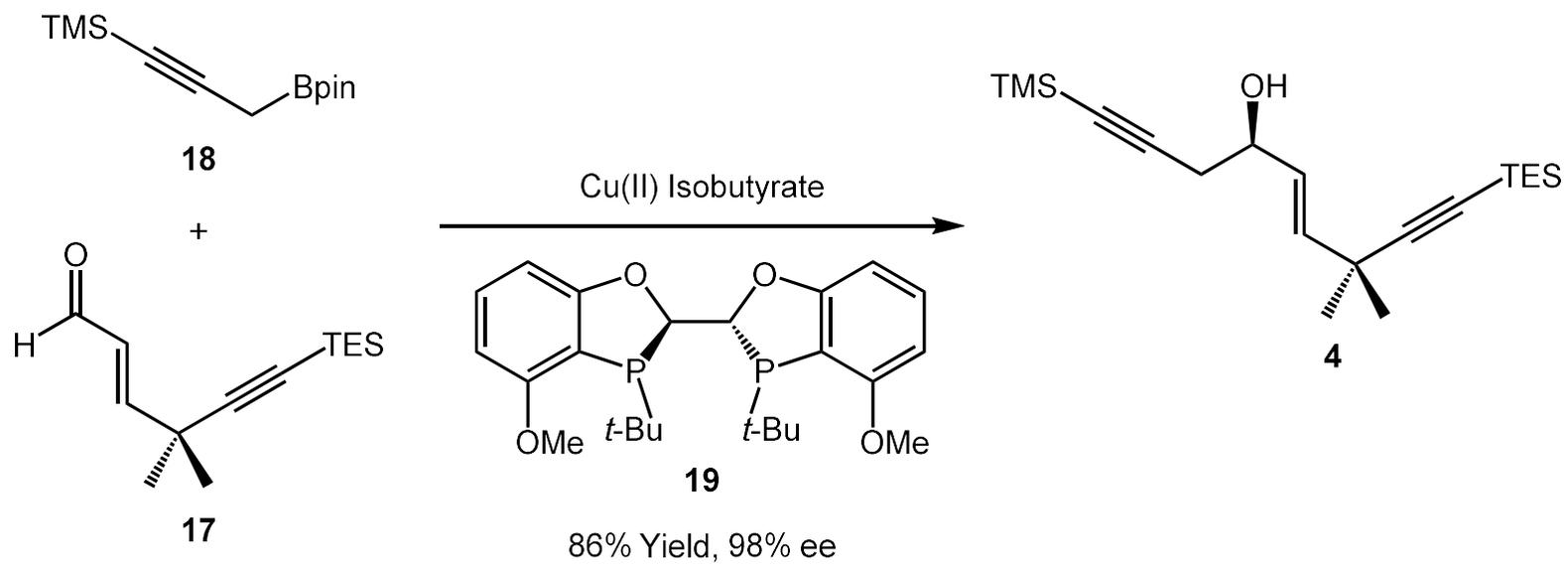


# Synthesis of Intermediate 17

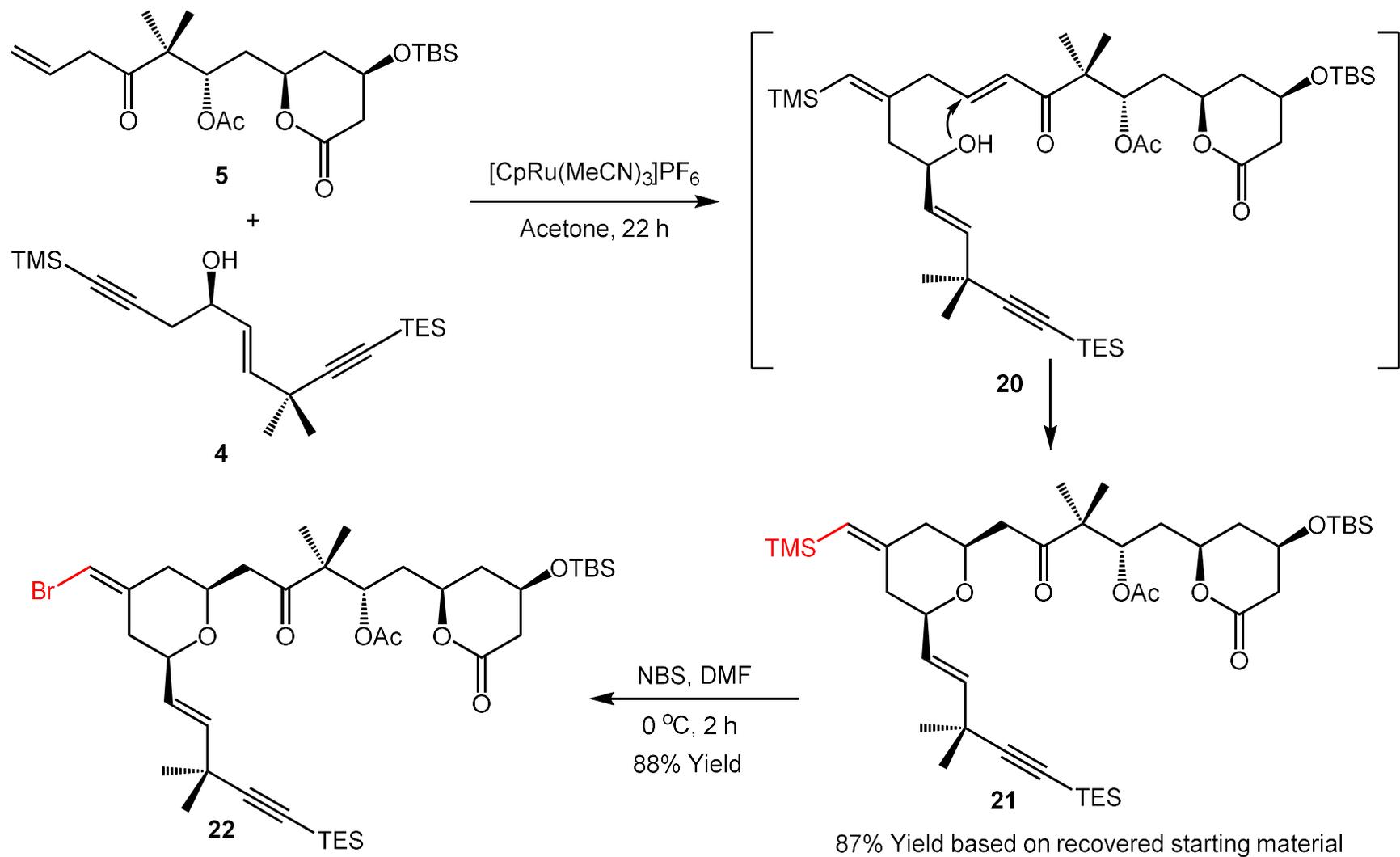


# Synthesis of Intermediate 4

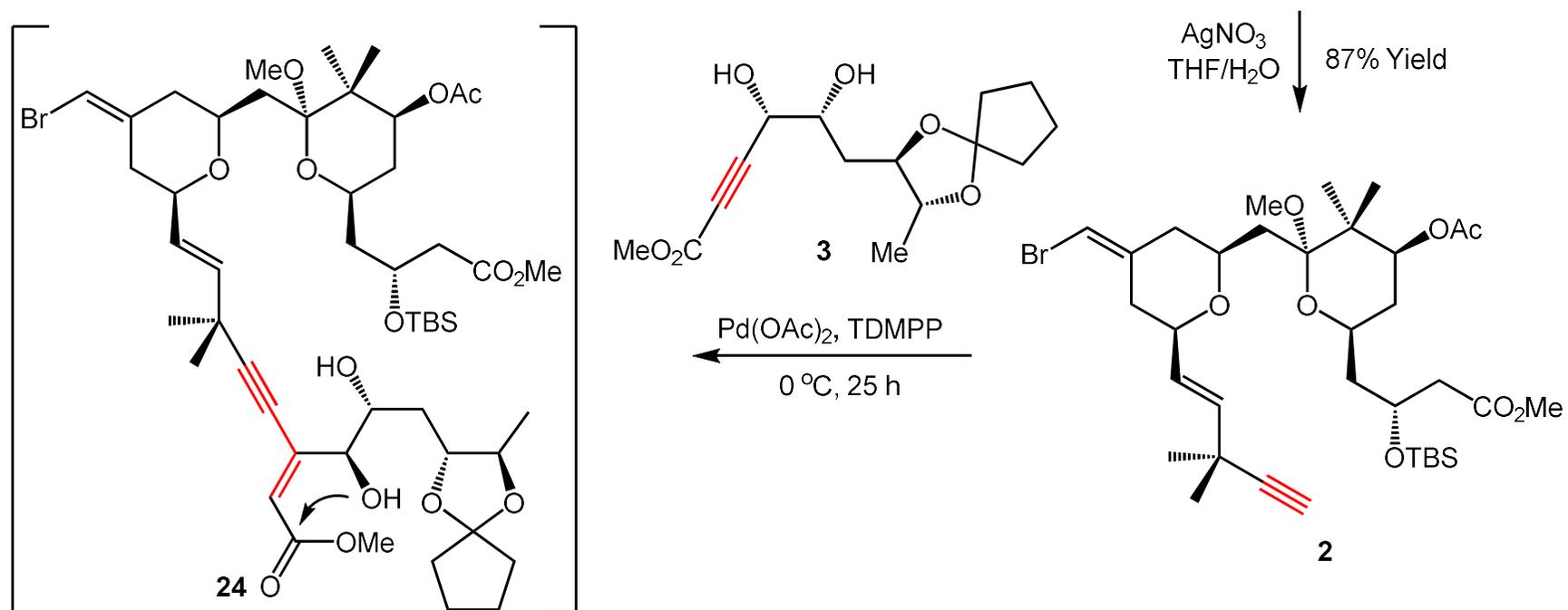
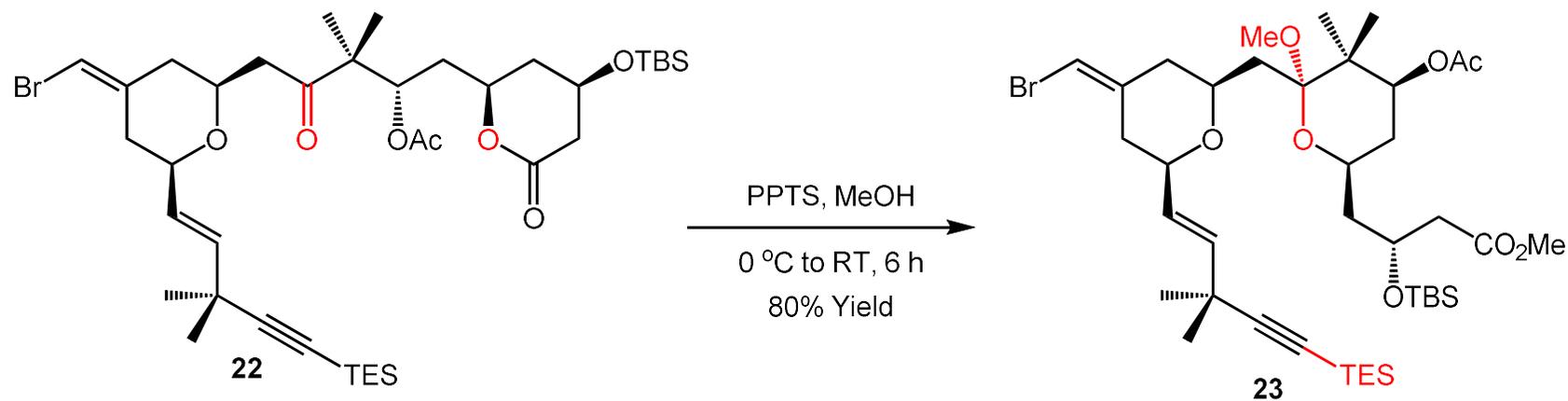
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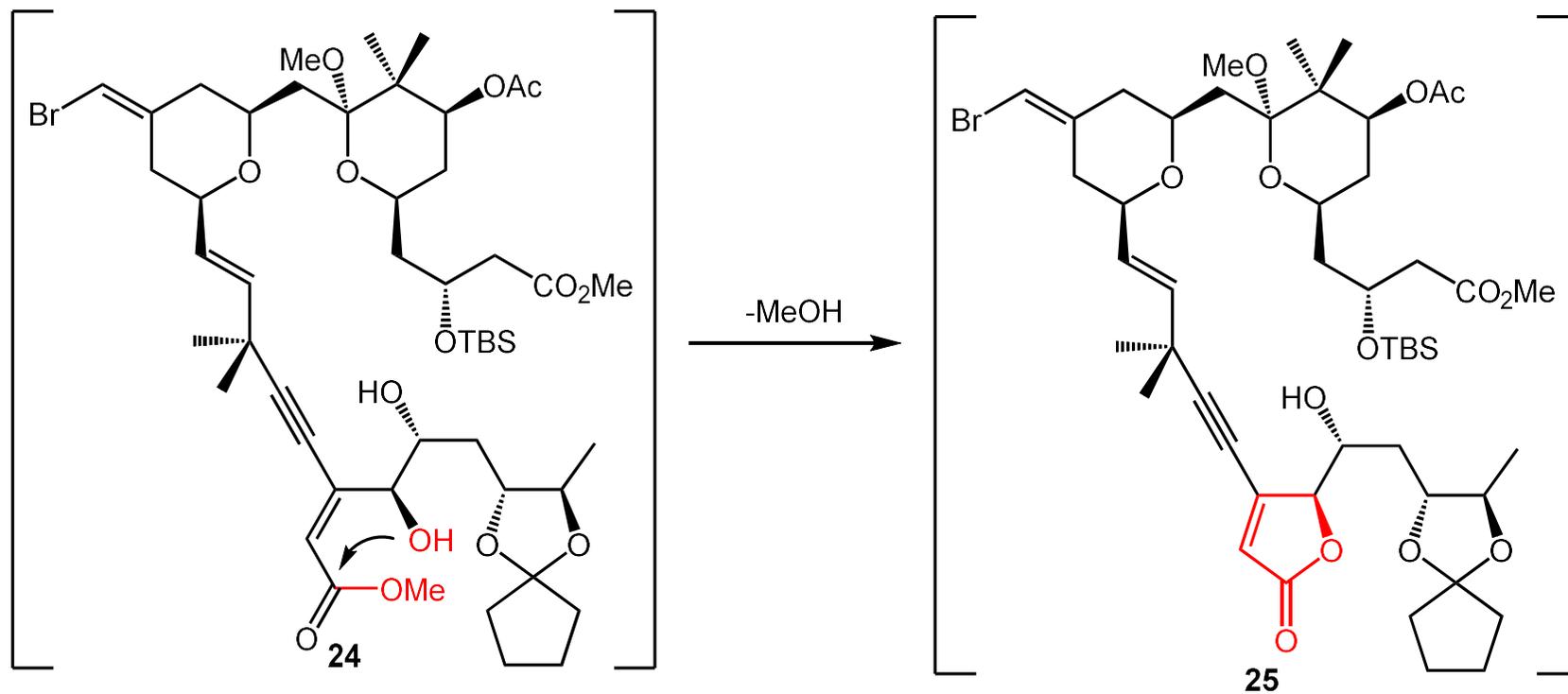
# Synthesis of Intermediate 21



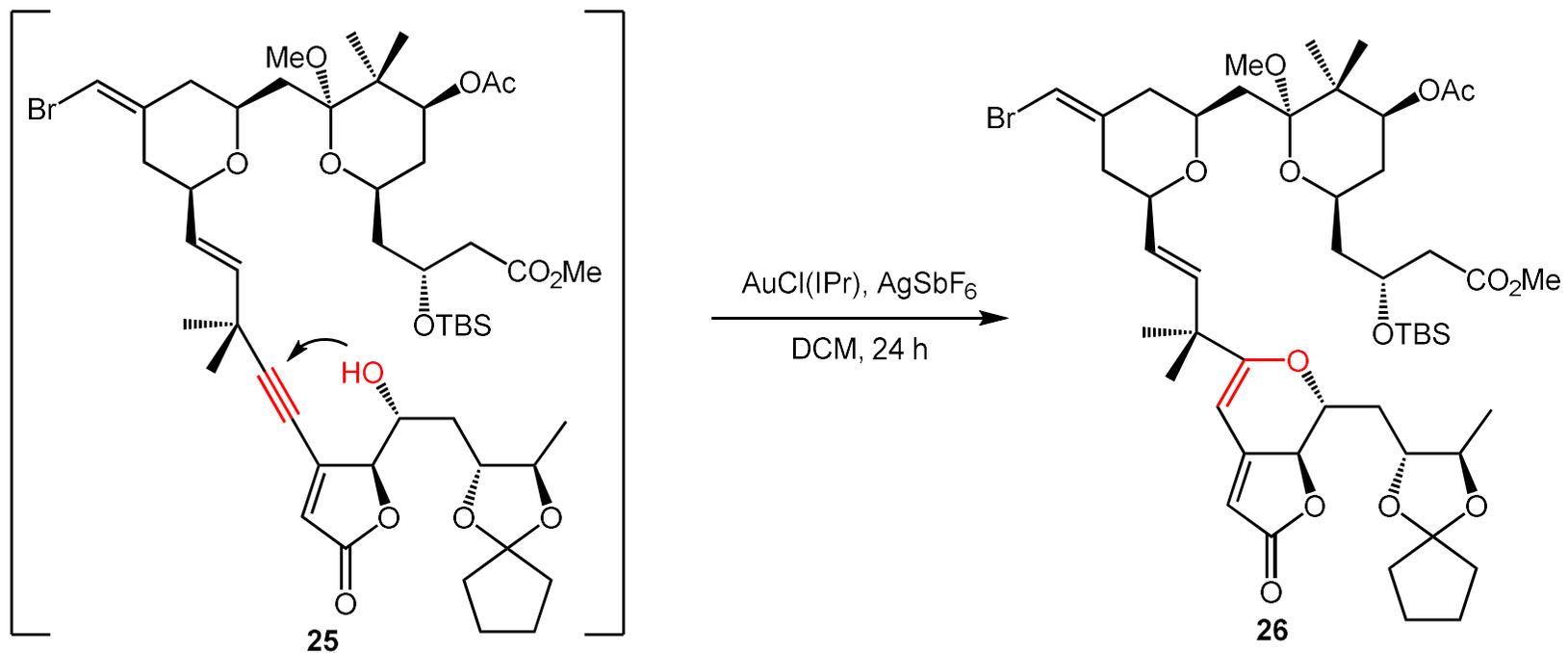
# Synthesis of Intermediate 26



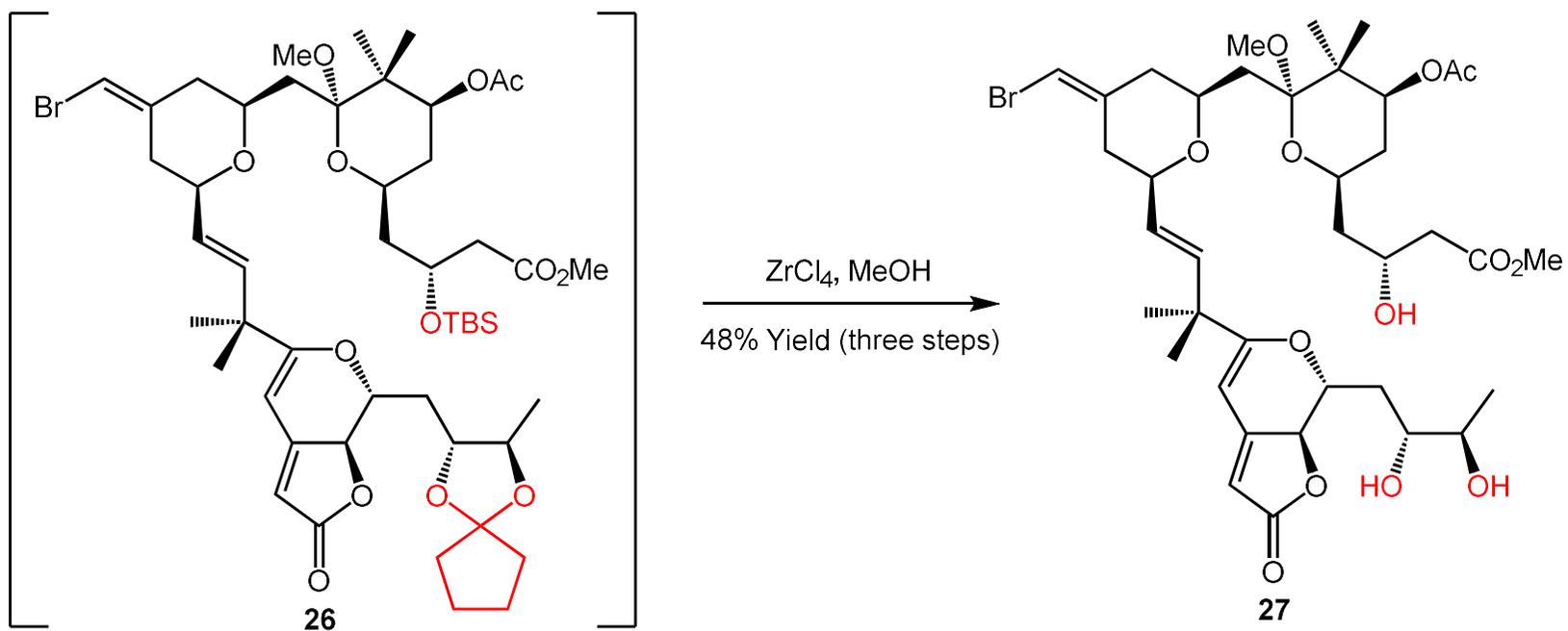
# Synthesis of Intermediate 26



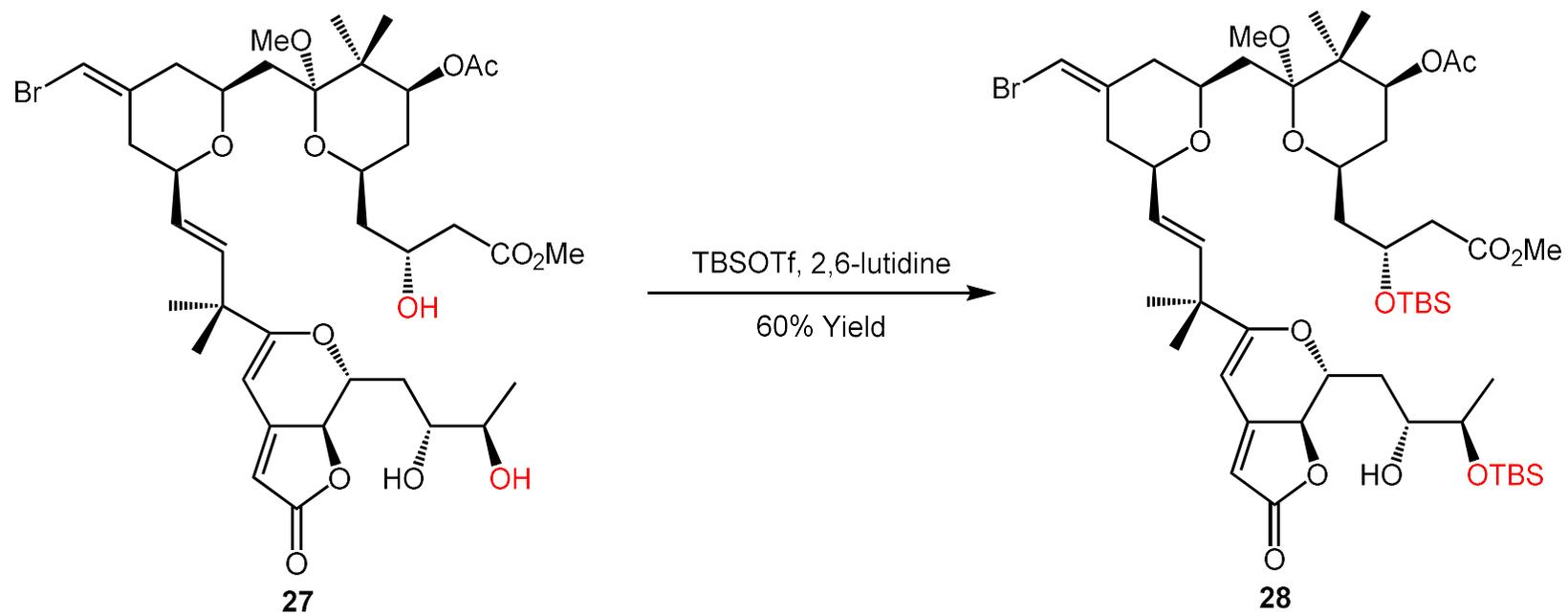
# Synthesis of Intermediate 26



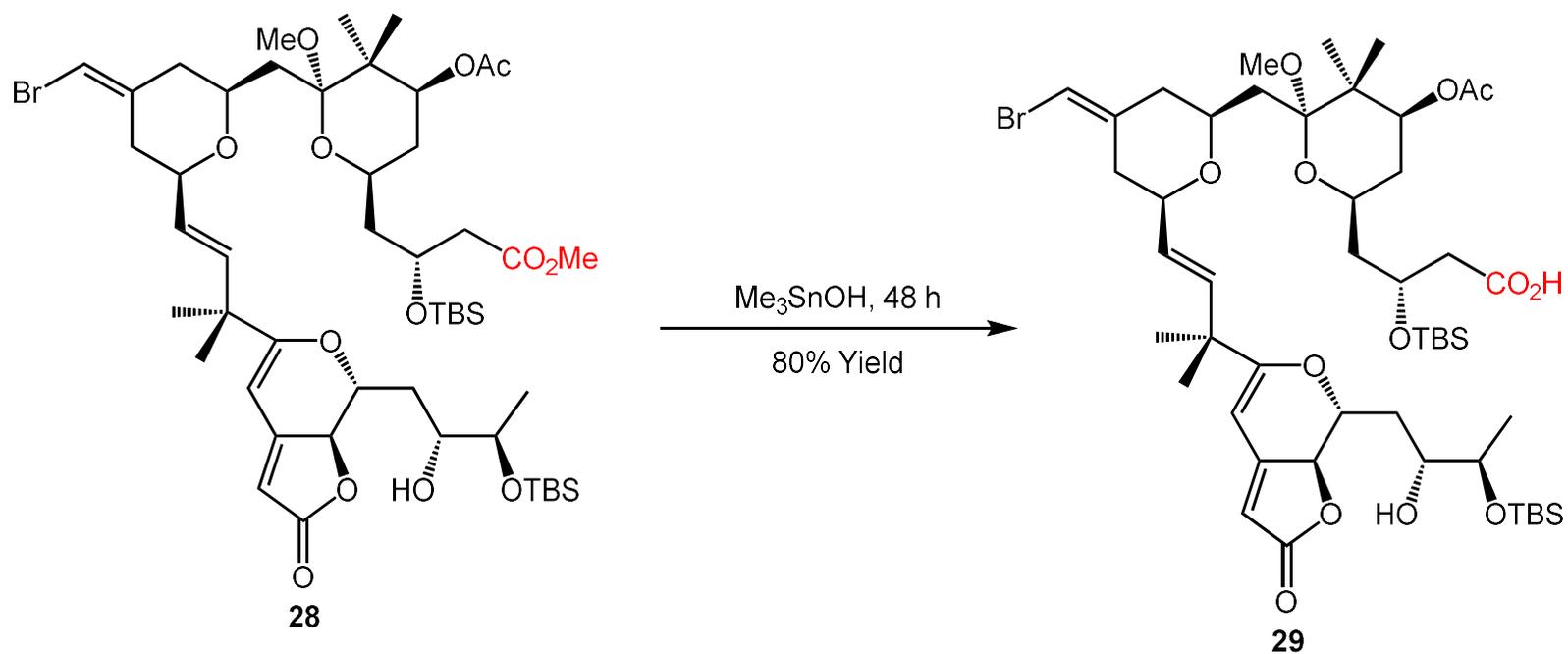
# Synthesis of Intermediate 27



# Synthesis of Intermediate 28

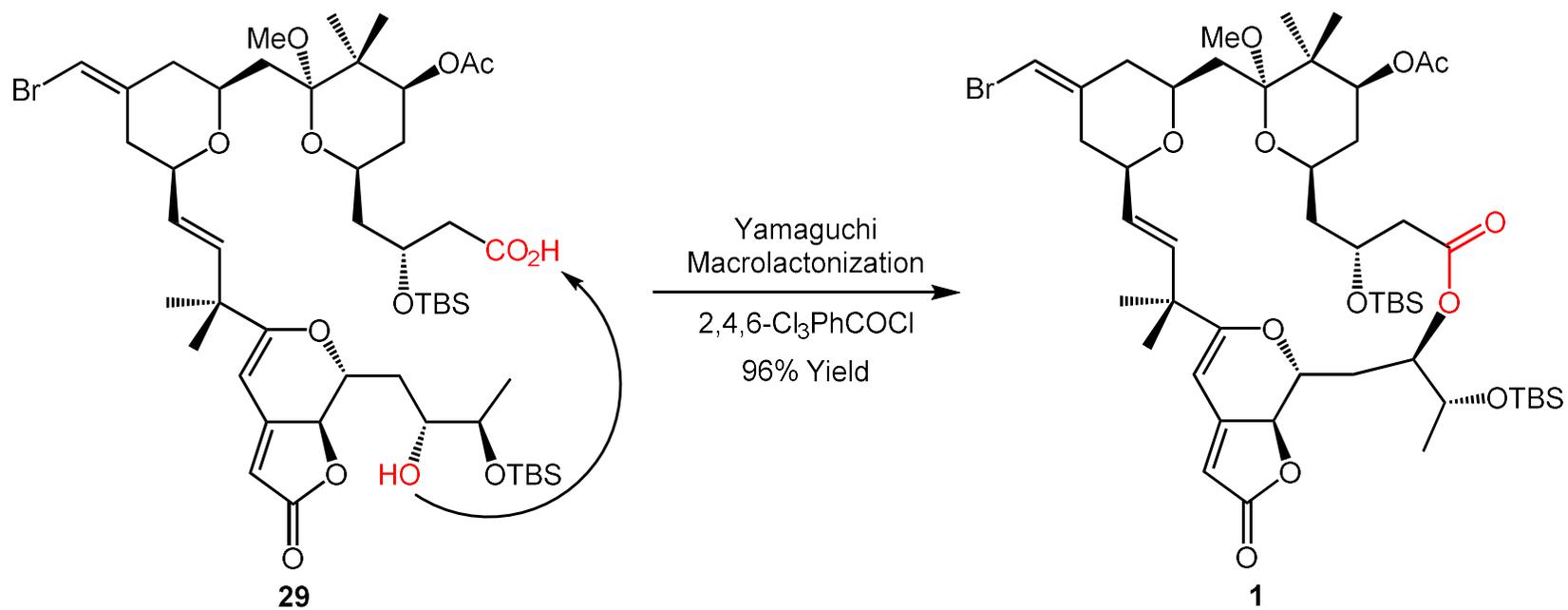


# Synthesis of Intermediate 29

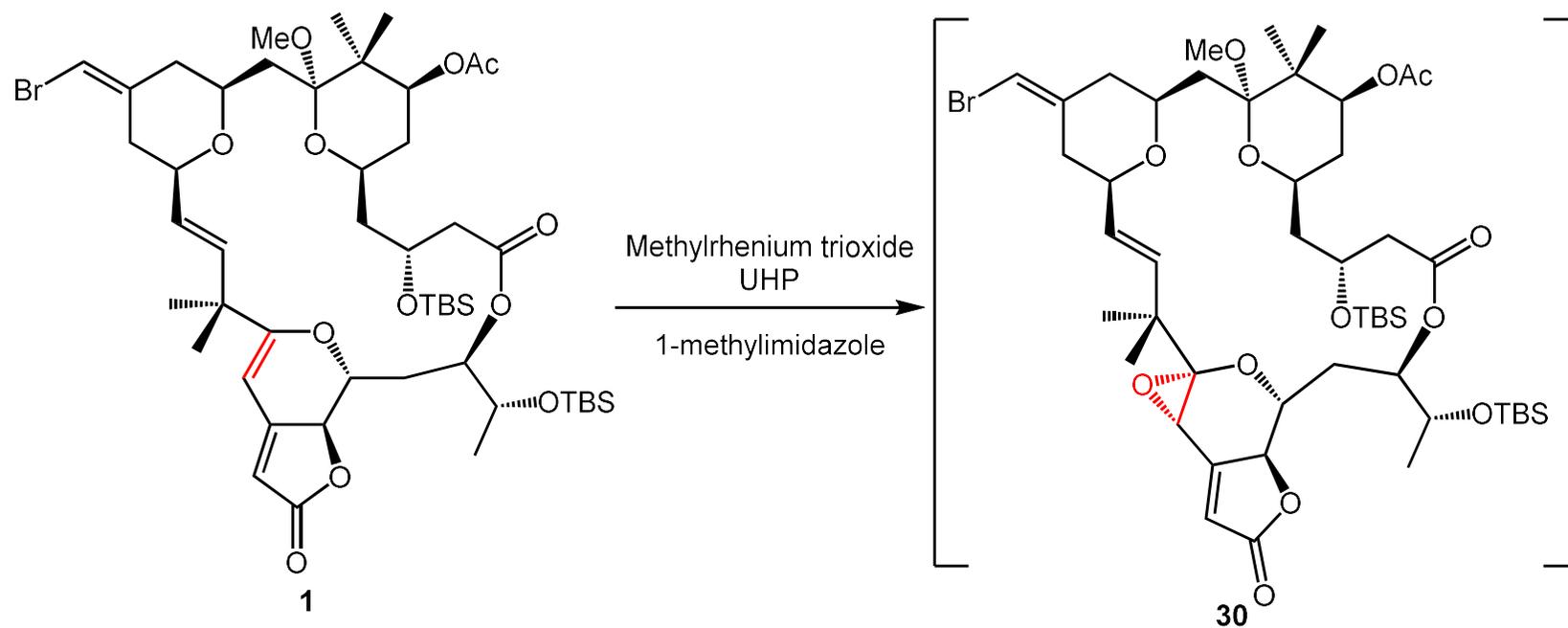


# Synthesis of Intermediate 1

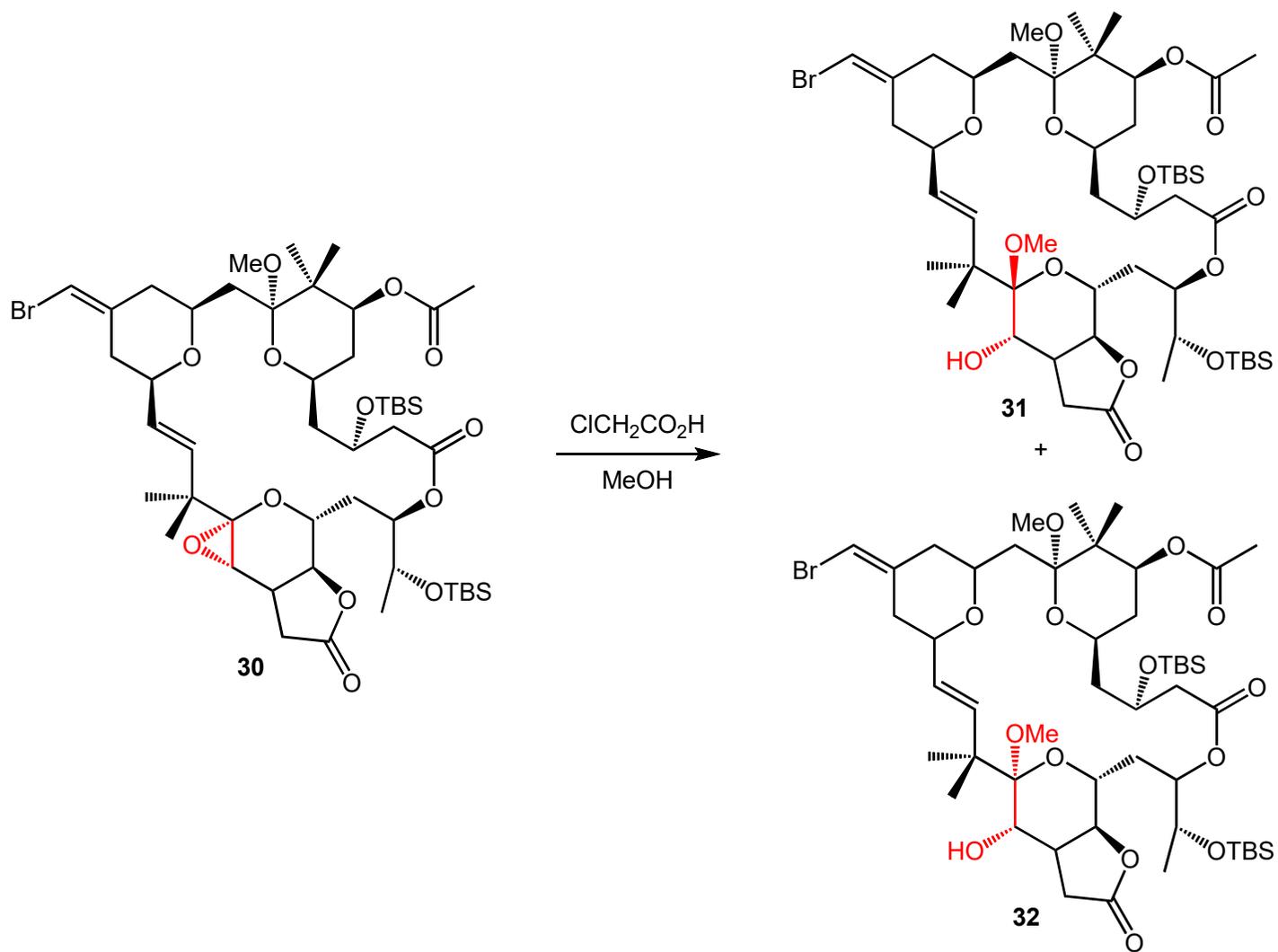
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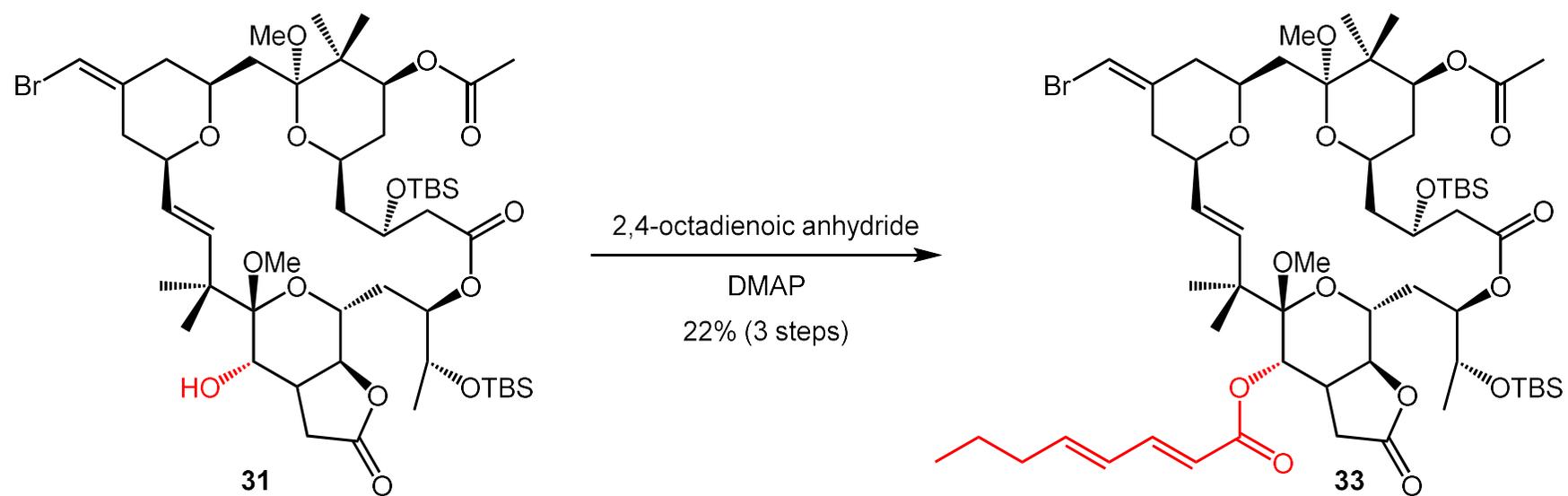
# Synthesis of Intermediate 33



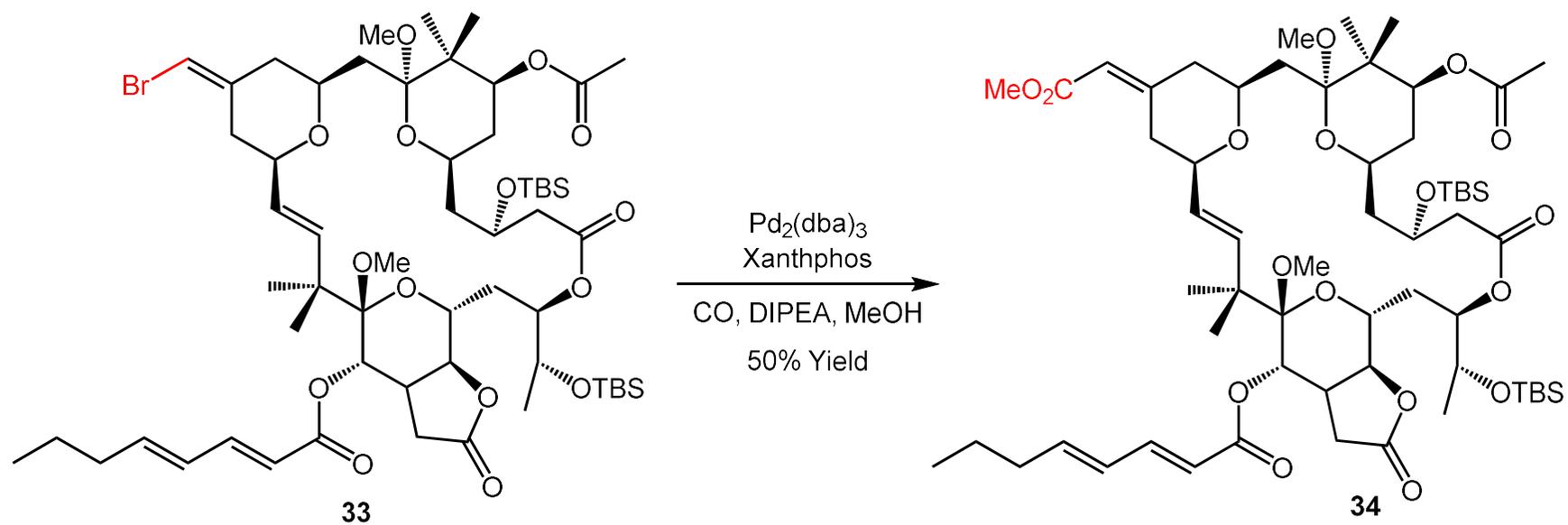
# Synthesis of Intermediate 33



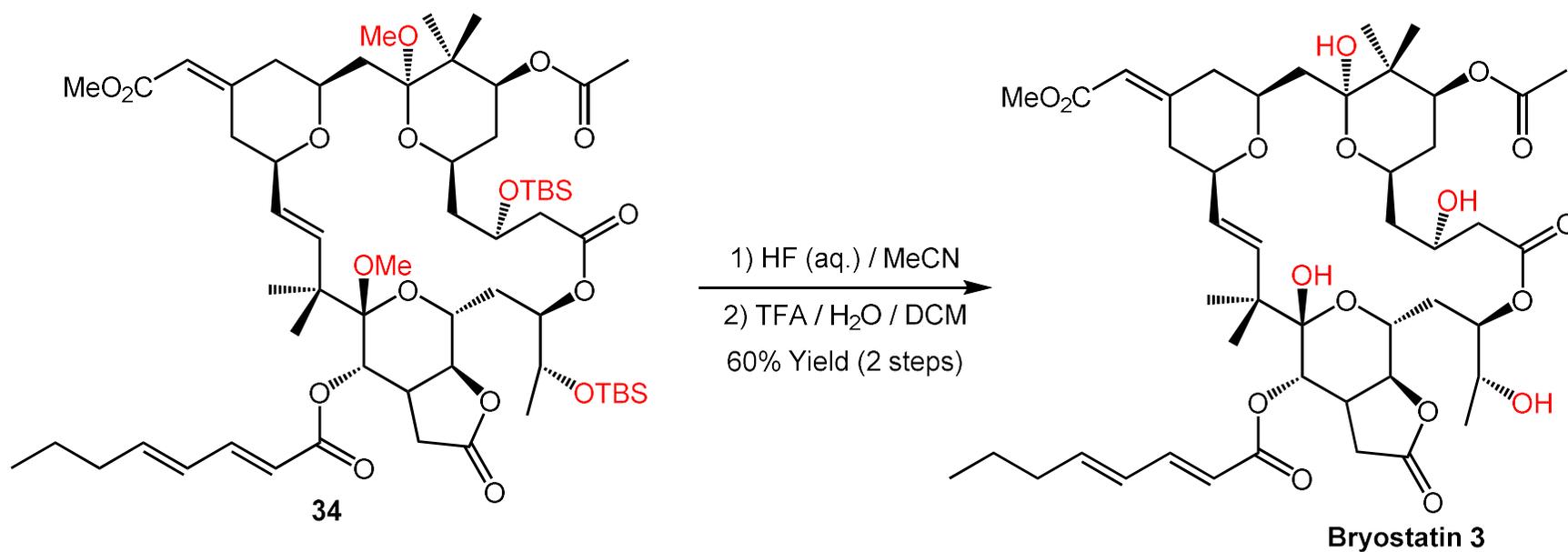
# Synthesis of Intermediate 33



# Synthesis of Intermediate 34



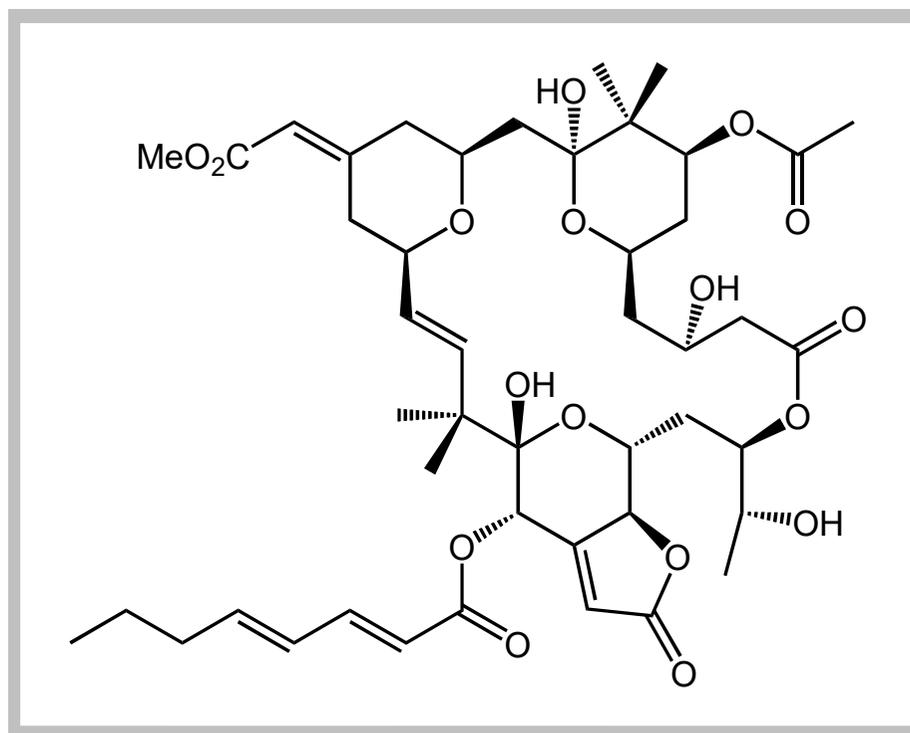
# Synthesis of Intermediate Bryostatin 3



# Summary

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22 (43) Steps in the longest linear sequence and 31 (88) total steps



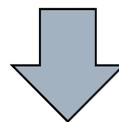
Palladium-catalyzed alkyne/alkyne coupling reaction; Yamaguchi macrolactonization; Ruthenium-catalyzed alkene/alkyne coupling reaction; Sharpless asymmetric dihydroxylation

# The First Paragraph

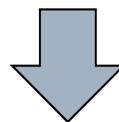
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写作思路:

天然产物来源



重要性



合成进展

# The First Paragraph

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The bryostatins, first isolated by Pettit *et al.* from the marine bryozoan, are a family of 21 macrolides with potent antineoplastic, immunopotentiating and latent HIV–modulating activity. Although the exact mechanism of action remains an ongoing area of research, it has become clear that bryostatins act as agonists of protein kinase C (PKC) with low nanomolar. Their pharmacological potential together with their intriguingly complex structures have attracted the attention of numerous synthetic organic chemists over the past 30 years.

# The First Paragraph

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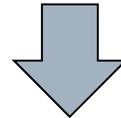
To date, nine completed total syntheses have been reported. In addition, Hale has developed a formal synthesis of bryostatin 7, and other groups also have made important contributions to this area. All of these synthetic studies serve as guidelines toward the ultimate goal of a concise route to bryostatins that is practical, and allowing for ready access to analogs for structure-activity-relationship (SAR) studies.

# The Last Paragraph

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写作思路:

完成了什么工作



未来工作展望

# The Last Paragraph

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This concise total synthesis show cases the value of the alkyne functionality that emanates from its chemoselectivity and its flexibility in elaborating the required structural details. **The synthetic strategy and synthetic technologies in this work are expected to have implications toward the ultimate goal of practical, flexible, and concise synthesis of bryostatins and their bioactive analogs.**

# Representative examples

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**Although** the exact mechanism of action **remains an ongoing** area of research, **it has become clear that** bryostatins act as agonists of protein kinase C (PKC), with low nanomolar affinities for their target.

**To date**, nine completed total syntheses **have been reported**:

**Their** pharmacological potential together with their intriguingly complex structures **have attracted the attention of** numerous synthetic organic chemists over the past 30 years.

# Acknowledgement

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***Thanks***  
***for your kind attention !***