

Literature Report VIII

Asymmetric Total Synthesis of Pre-schisanartanin C

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Checker: Chang-Bin Yu

Date: 2020-06-09

Yang, Z. *et al. J. Am. Chem. Soc.* **2020**, *142*, 573–580.

CV of Prof. Zhen Yang



Zhen Yang

Background:

- ❑ **1978-1986** B.S. & M.S., Shenyang Pharmaceutical University
- ❑ **1989-1992** Ph.D., The Chinese University of Hong Kong
- ❑ **1992-1995** Postdoctoral, Scripps Research Institute
- ❑ **1995-1998** Assistant Professor, Scripps Research Institute
- ❑ **1998-2001** Institute Fellow, Harvard University
- ❑ **2001-present** Professor, Peking University

Research:

Developing novel synthetic methodologies and strategies, then applying them to the syntheses of complex natural products.

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Introduction

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First Generation of Synthetic Strategy

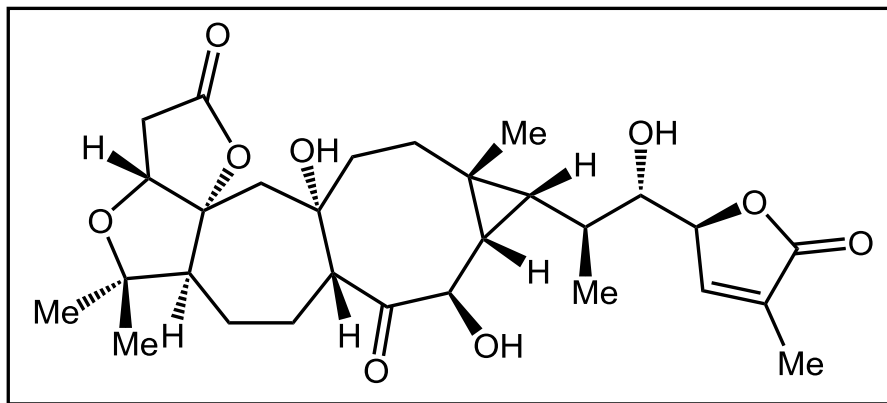
3

Second Generation of Synthetic Strategy

4

Summary

Introduction



Pre-schisanartanin C (1)

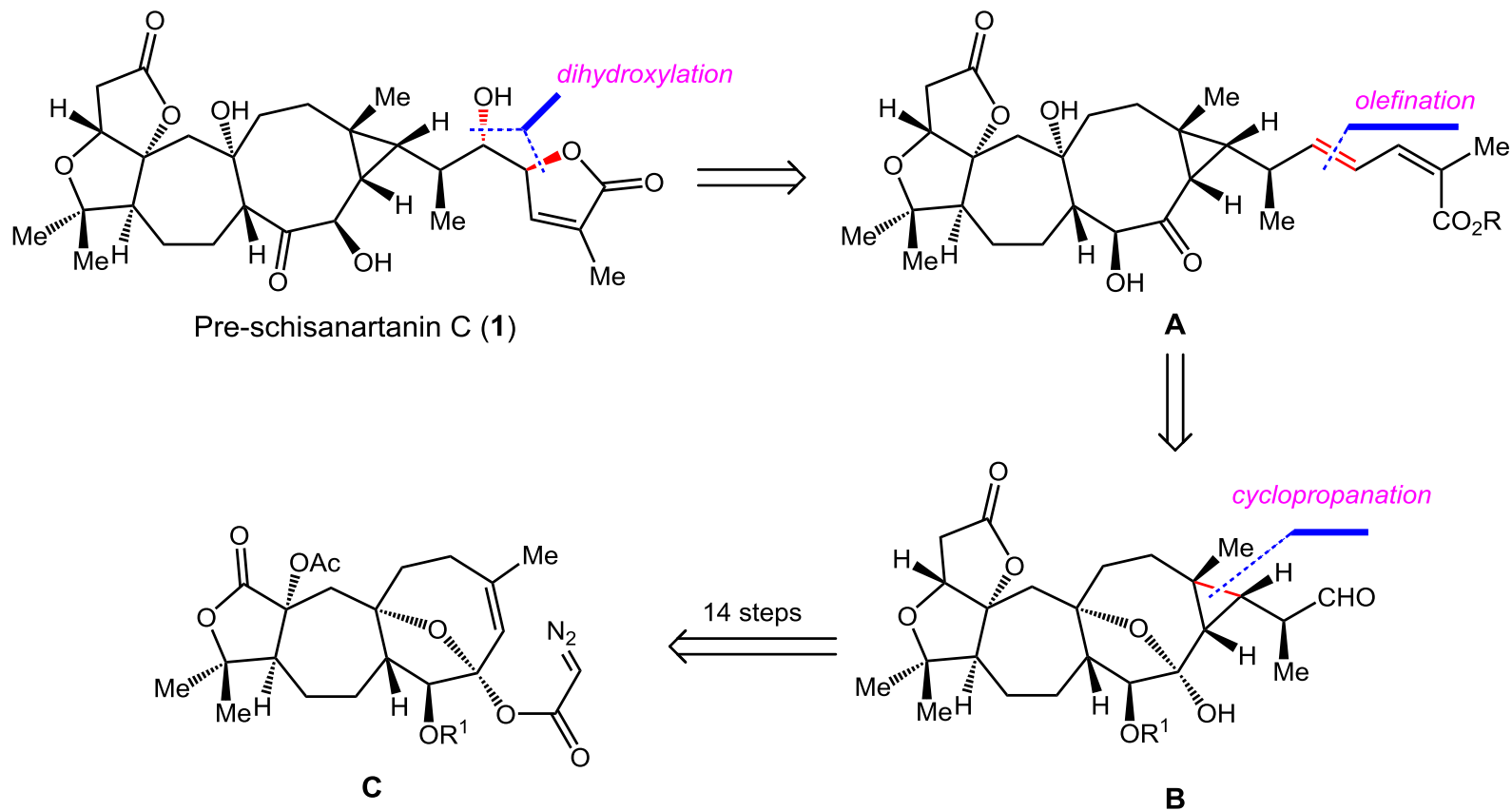


**Schisandra propinqua
var. propinqua**

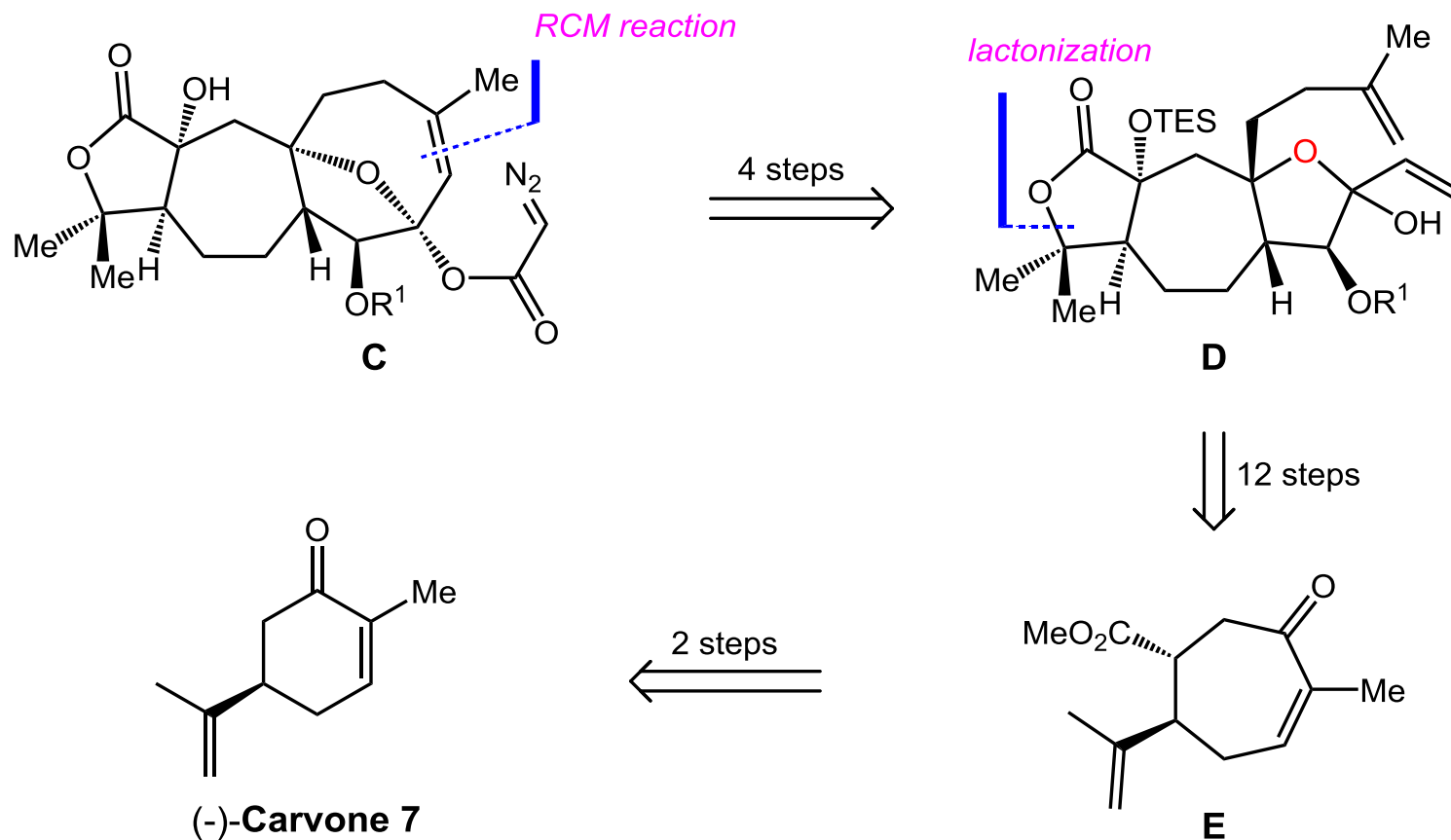
- Pre-schisanartanin C was isolated from the medicinal plant *Schisandra propinqua* var. *propinqua* by Sun and coworkers in 2010;
- It possessed 12 stereocenters, highly substituted bicyclo[6.1.0]nonane core and a highly labile α -hydroxy ketone motif;
- Its absolute configuration is still unknown.

Sun, H.-D. *et al. Tetrahedron* **2010**, 66, 2306.

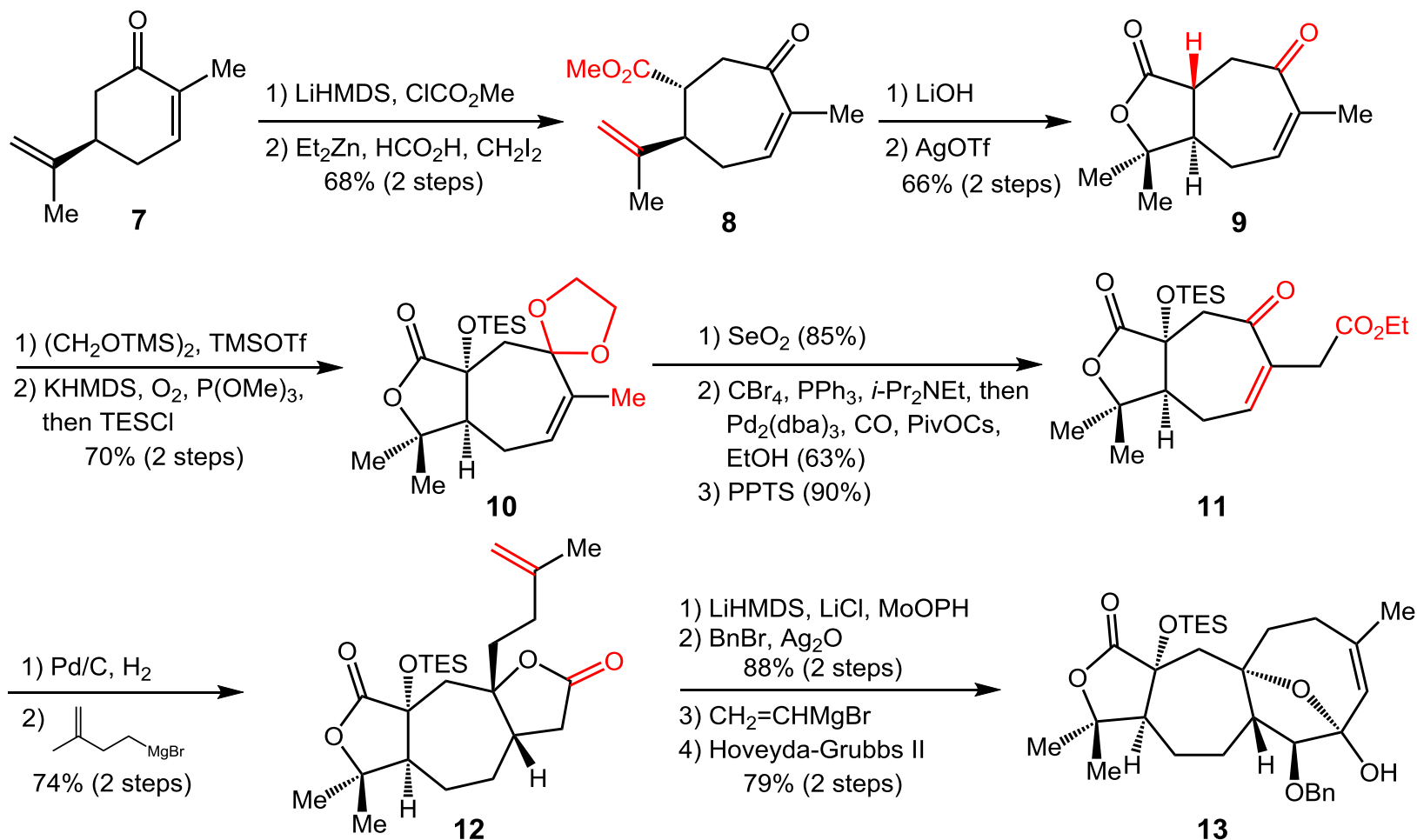
Retrosynthetic Analysis of 1- First Generation



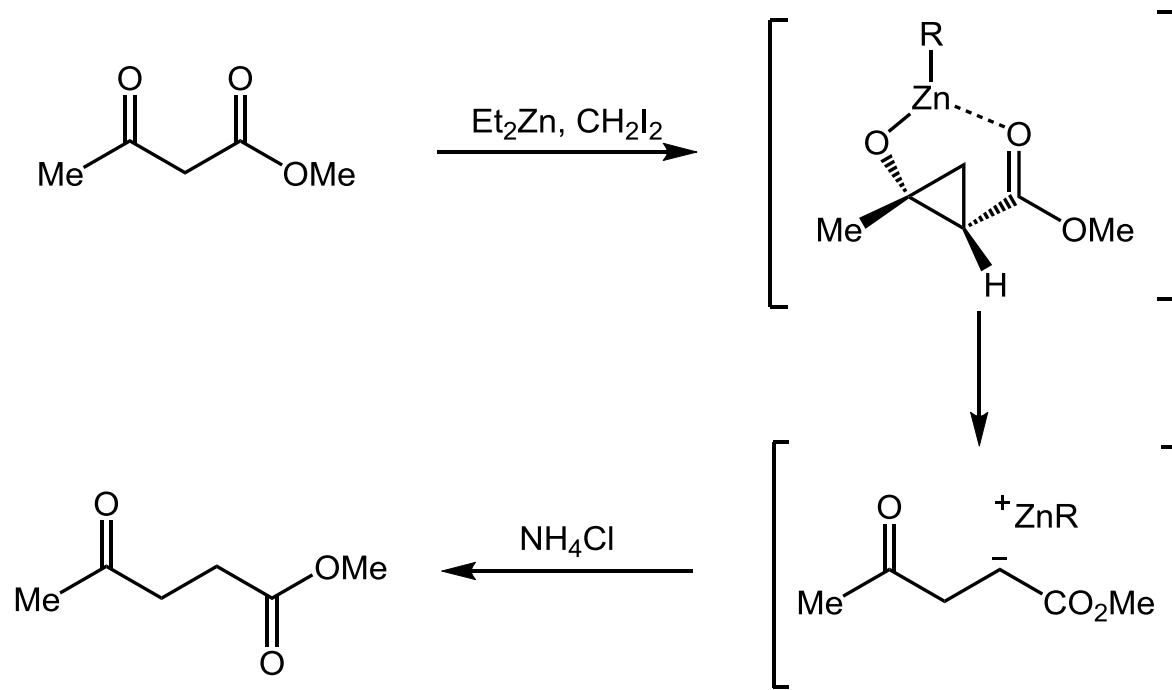
Retrosynthetic Analysis of 1- First Generation



Synthesis of compound 13

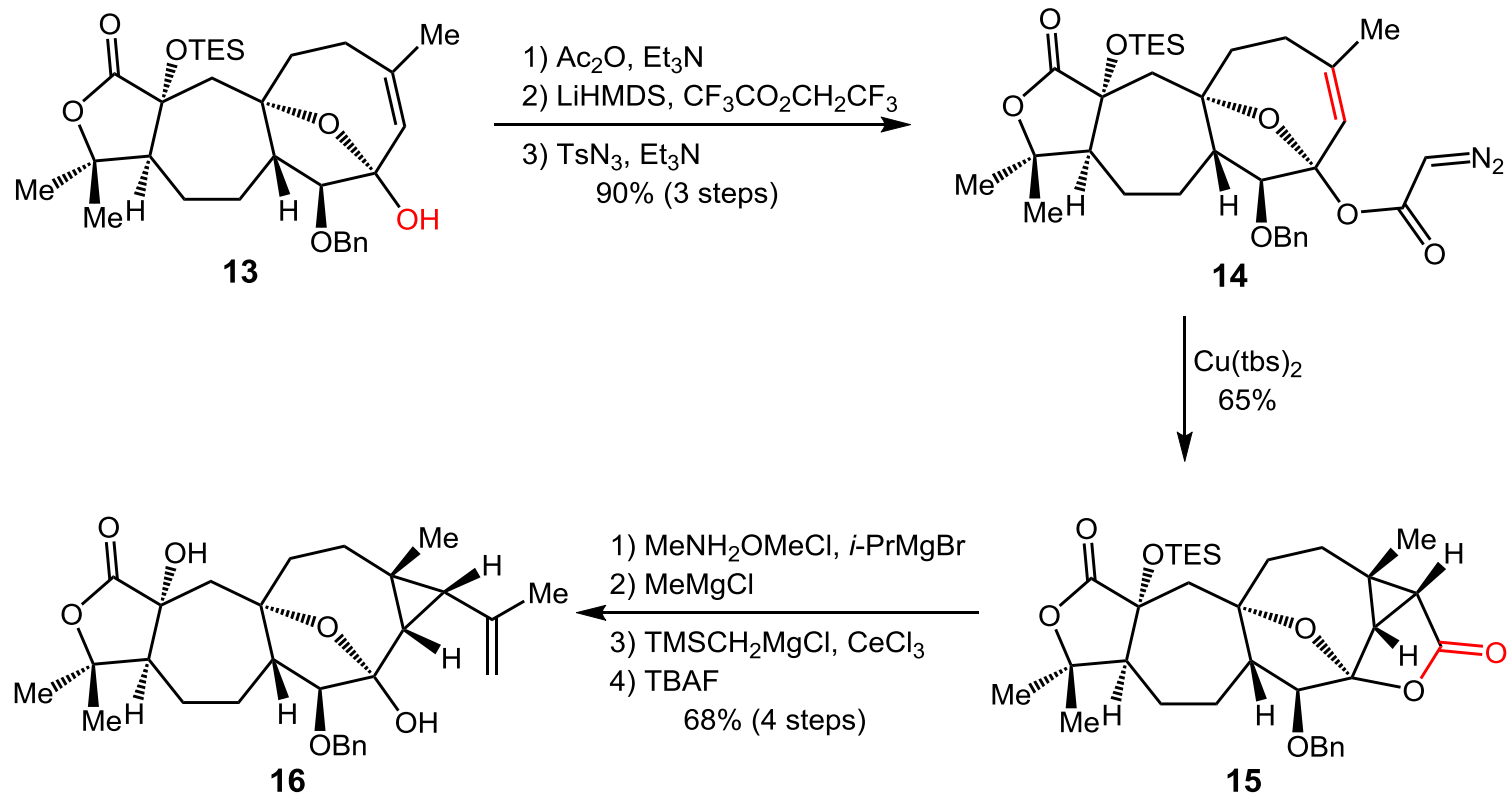


β -keto ester homologation protocol

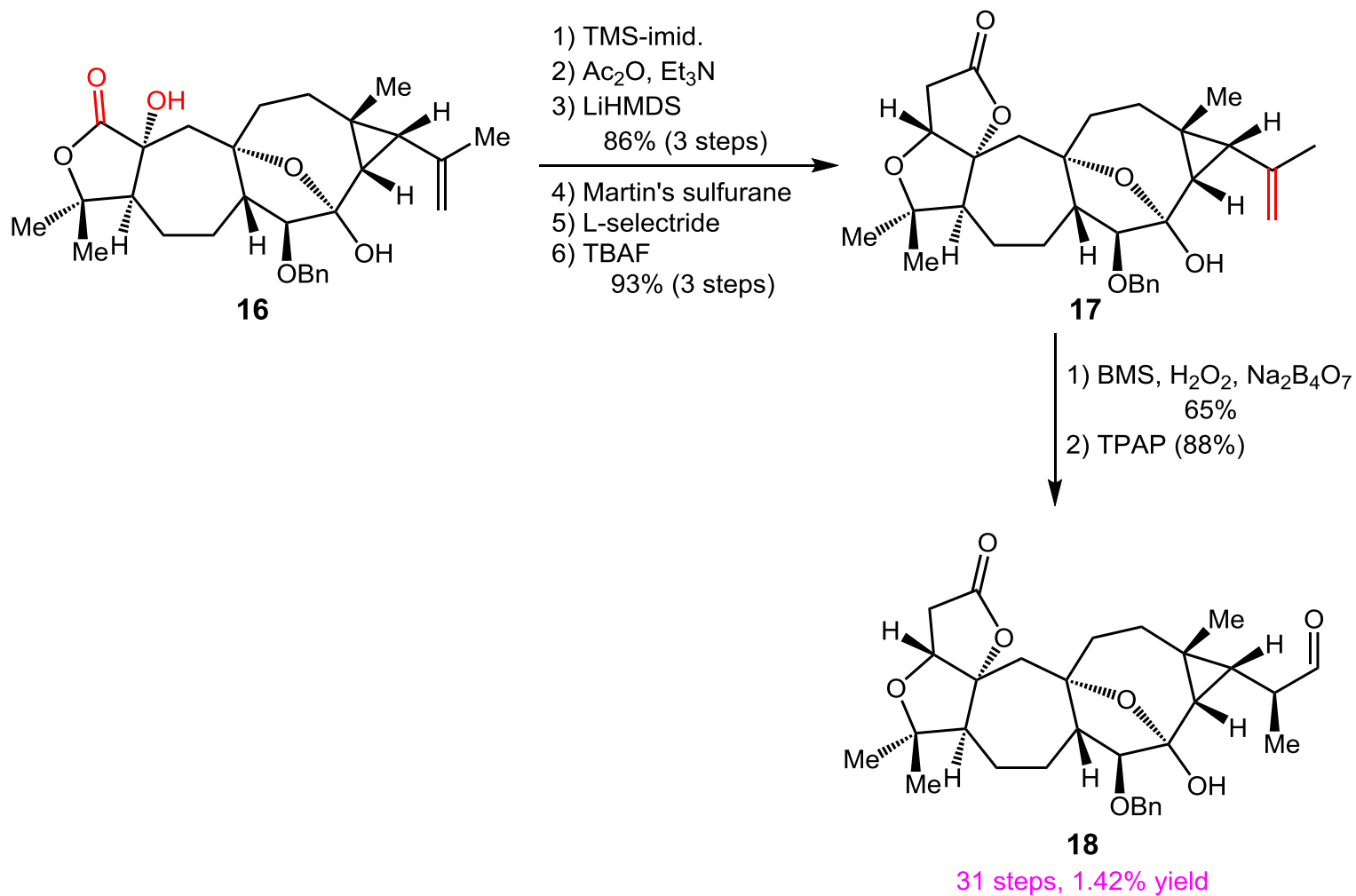


Zercher, C. K. *et al. J. Org. Chem.* **1997**, 62, 6444.

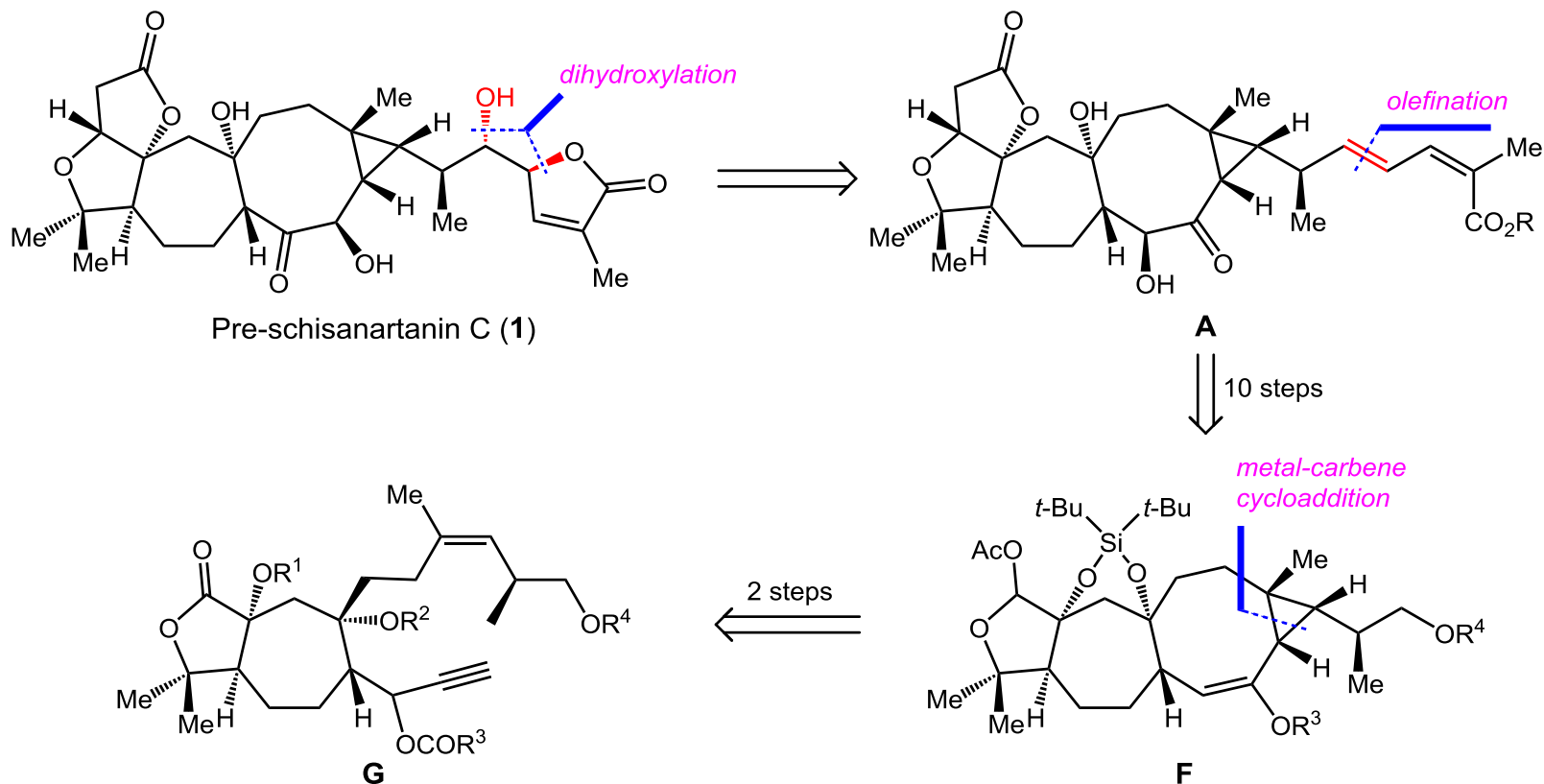
Synthesis of 16



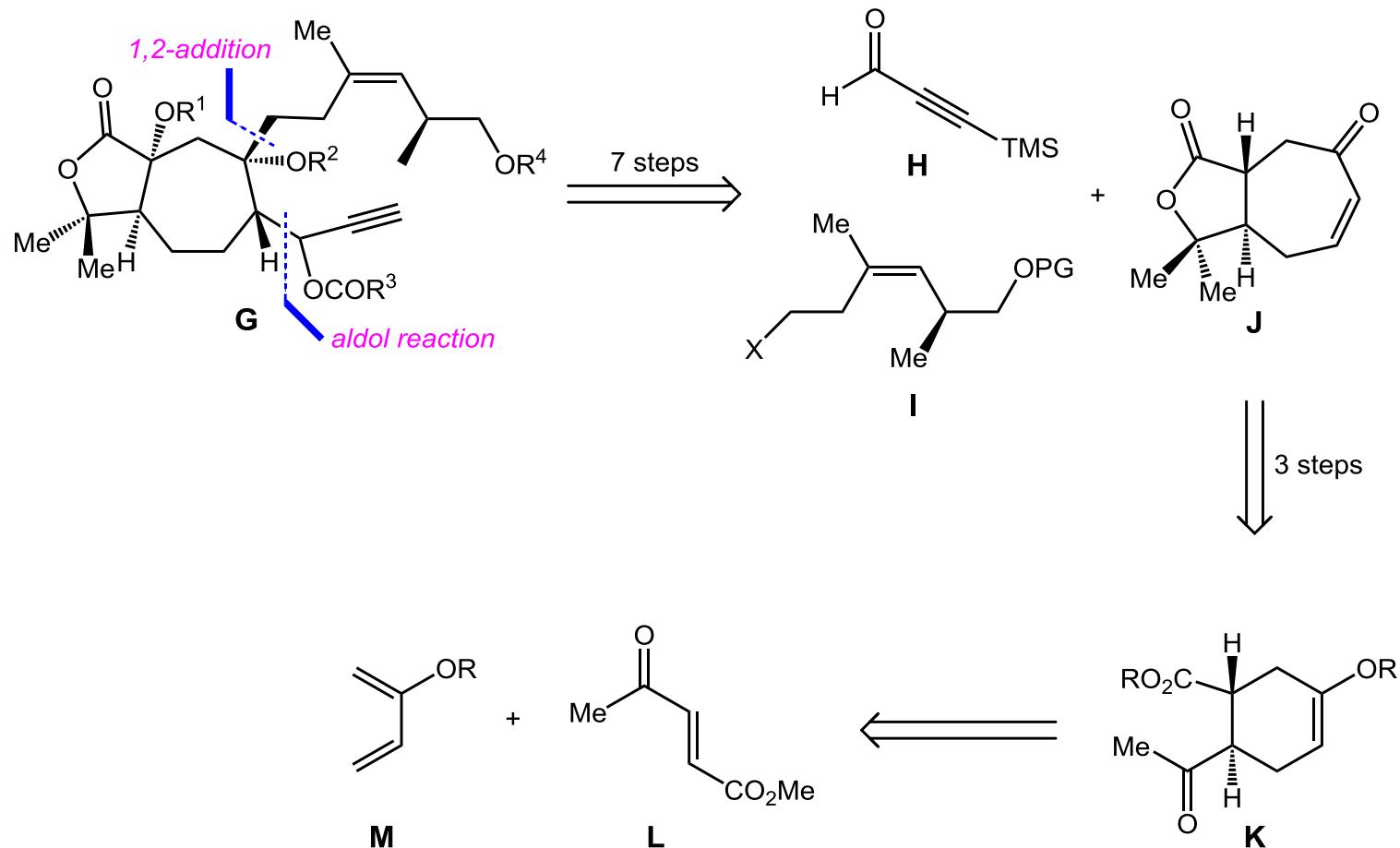
Synthesis of Aldehyde 18



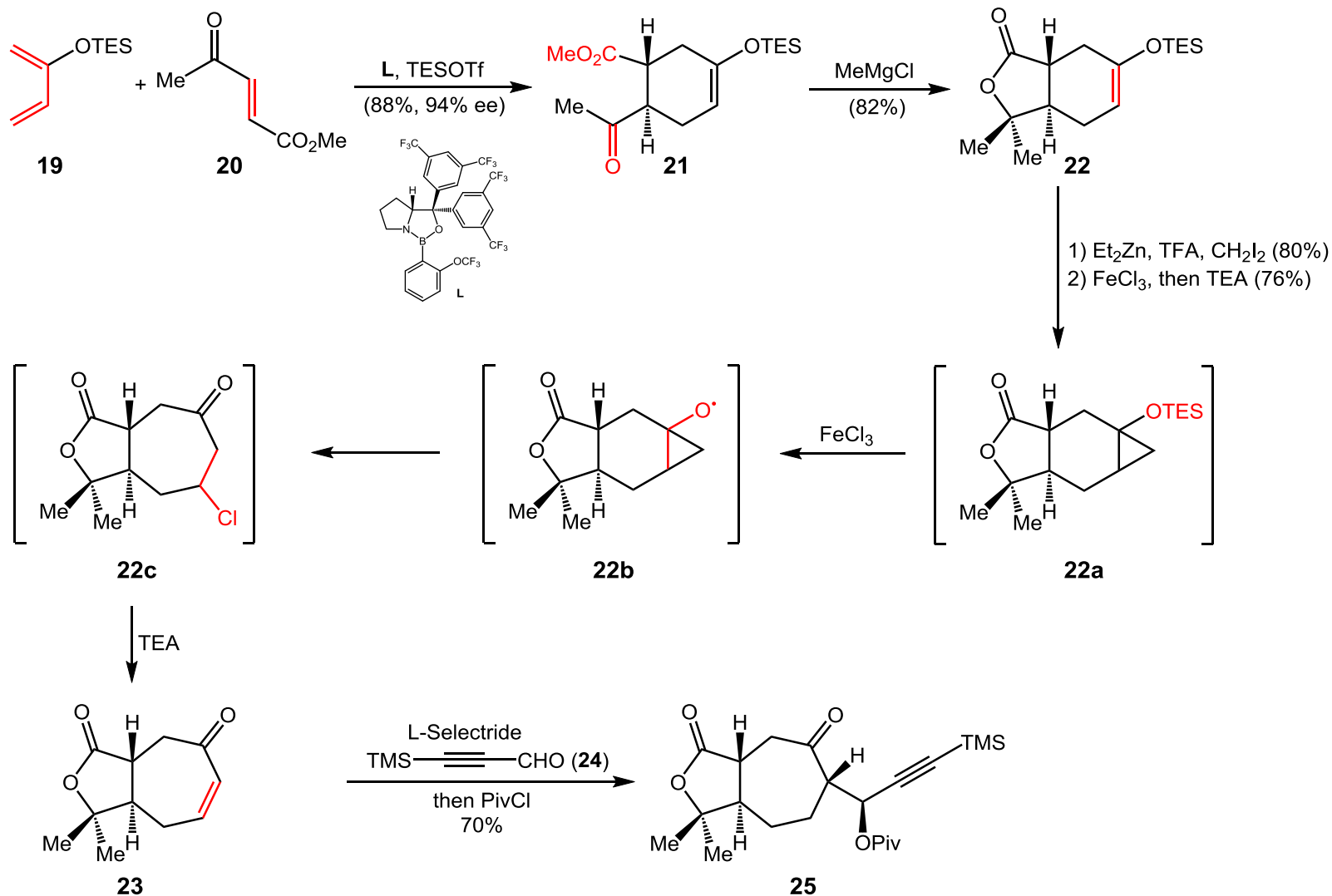
Retrosynthetic Analysis of 1- Second Generation



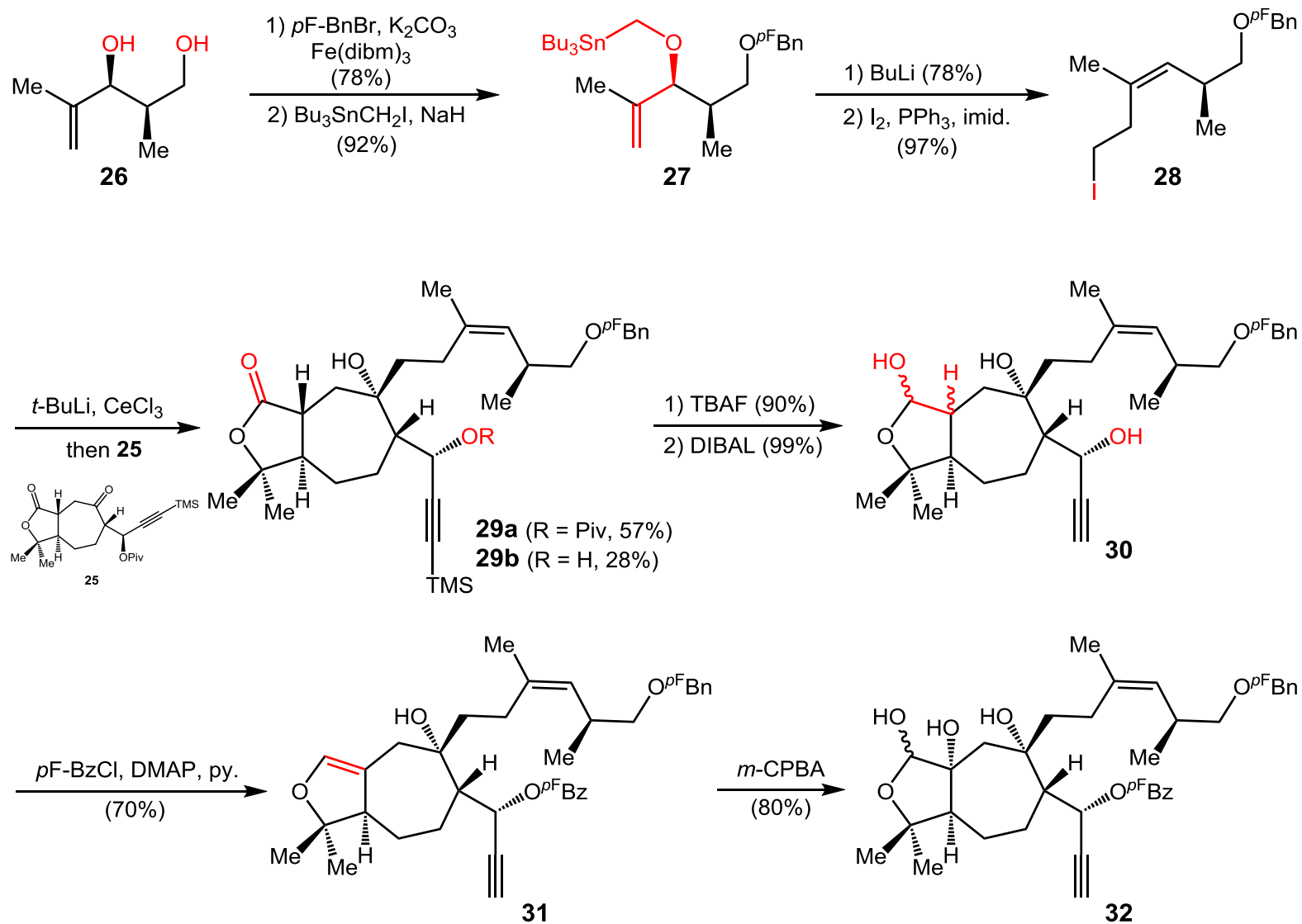
Retrosynthetic Analysis of 1- Second Generation



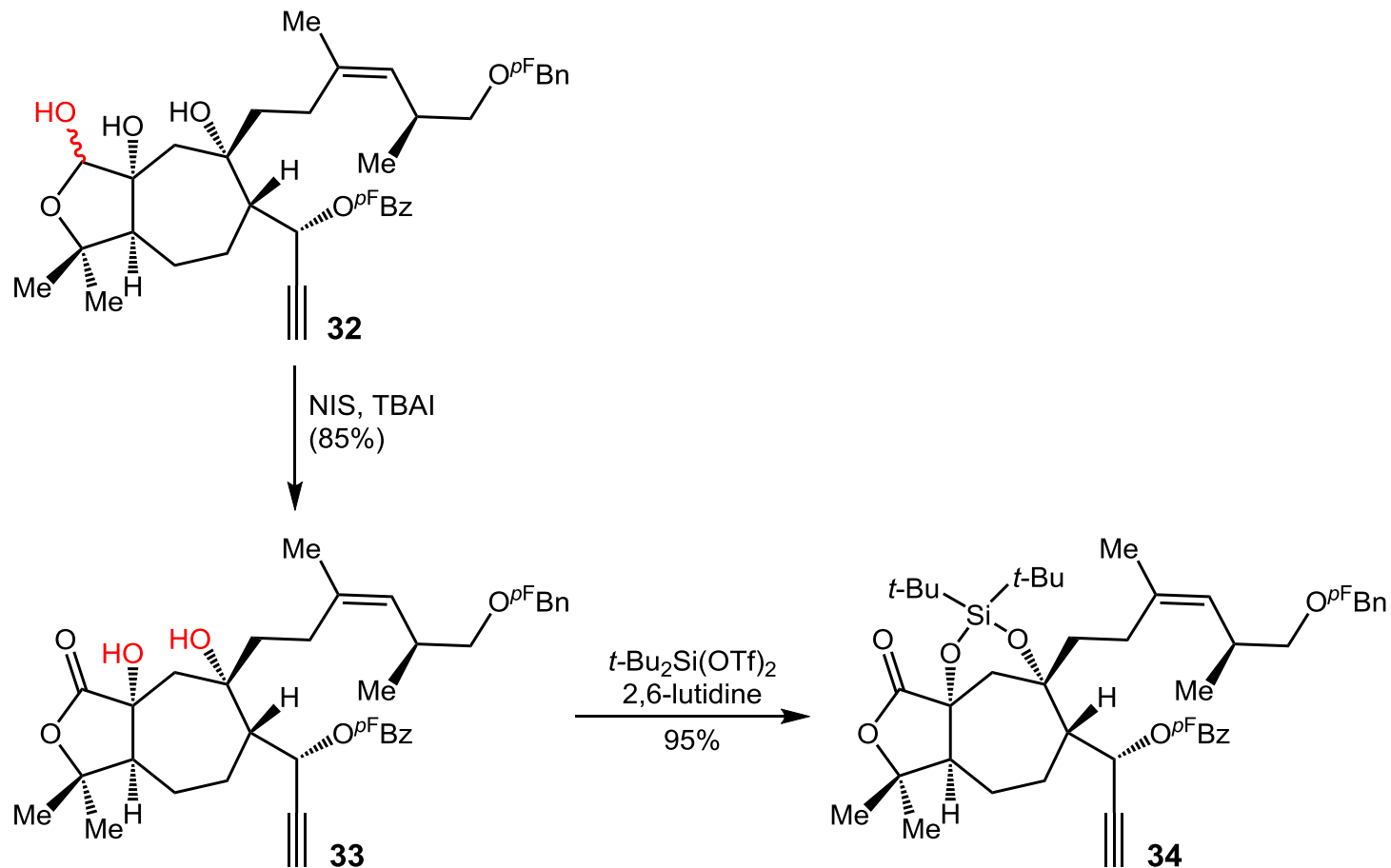
Synthesis of Compound 25



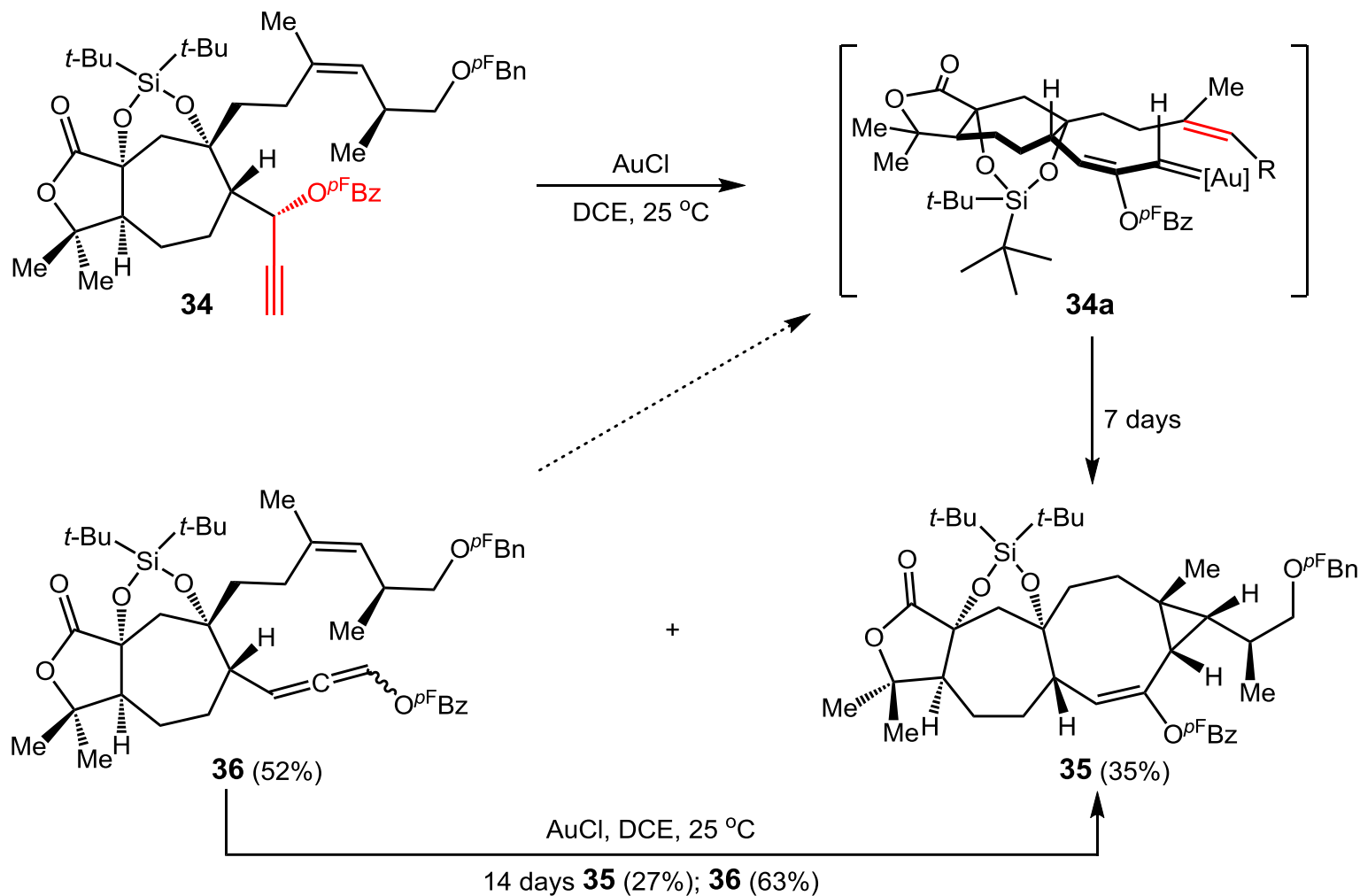
Synthesis of 32



Synthesis of Enyne 34



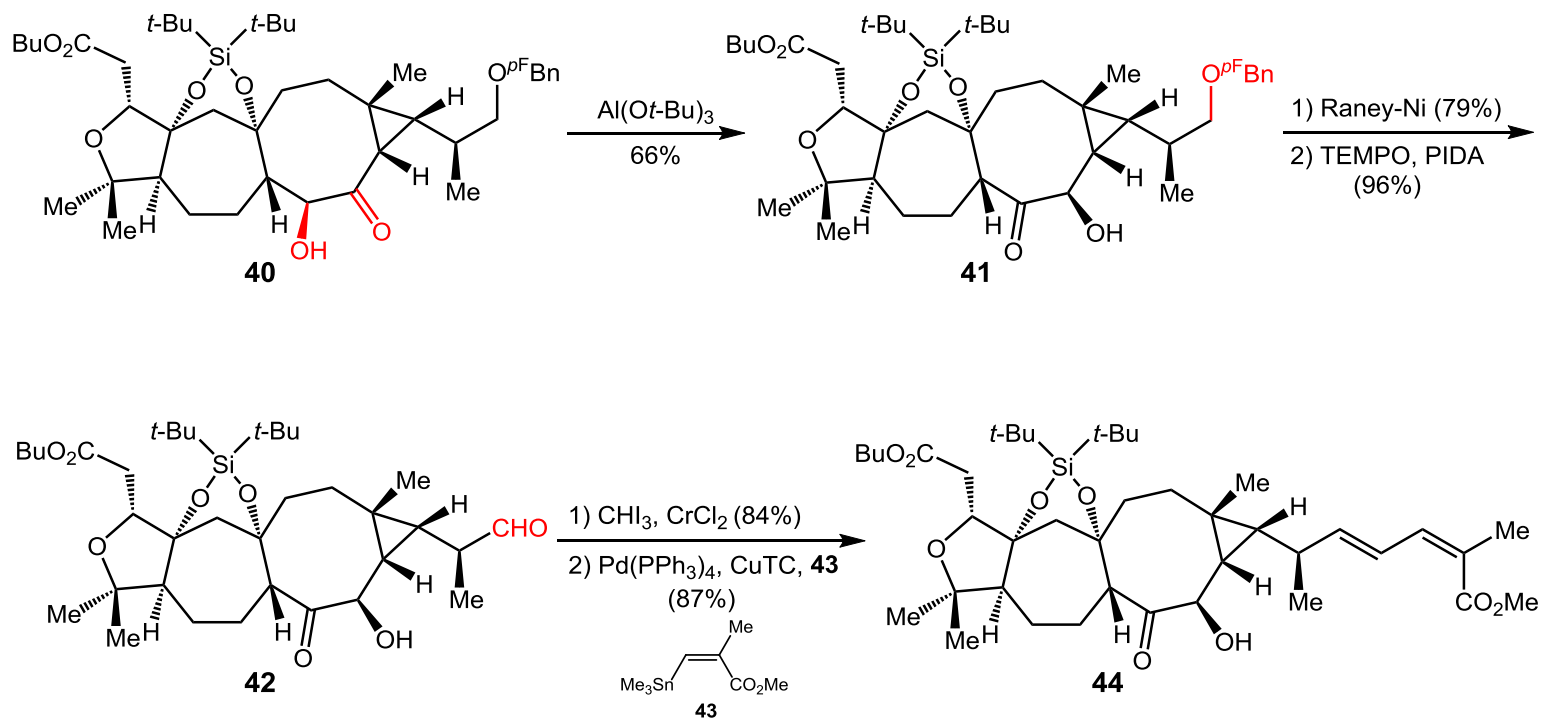
Au-Catalyzed Enyne Cyclization



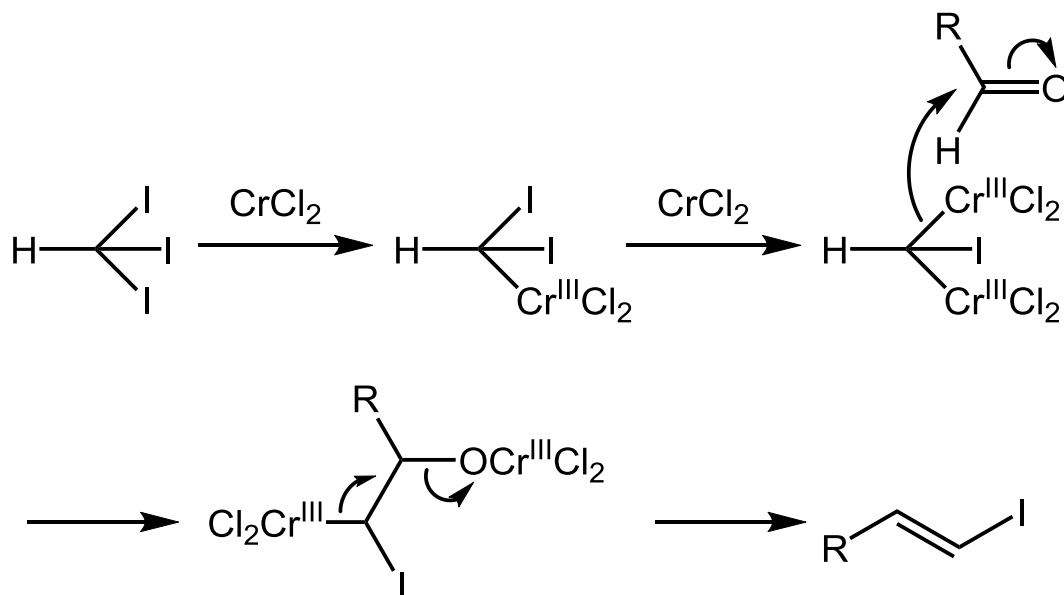
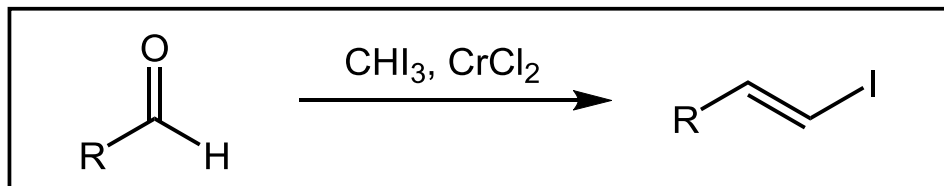
[illegible]

[illegible]

Synthesis of diene 44

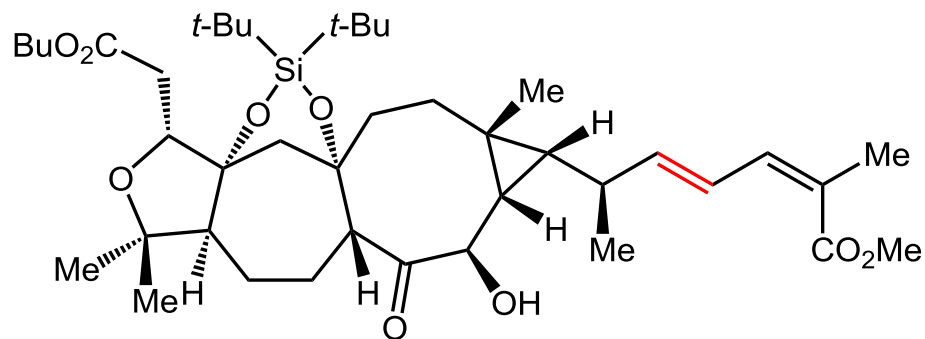


Takai Reaction



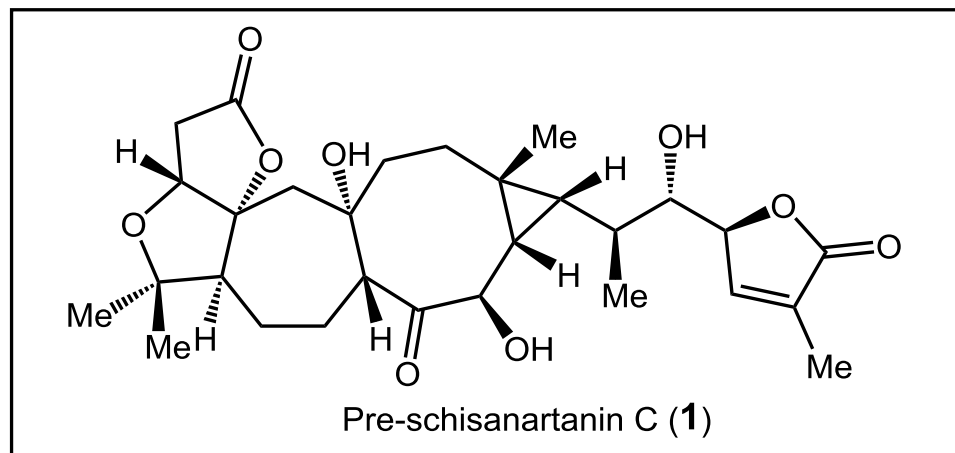
From Name Reactions

Completion of the Synthesis of 1



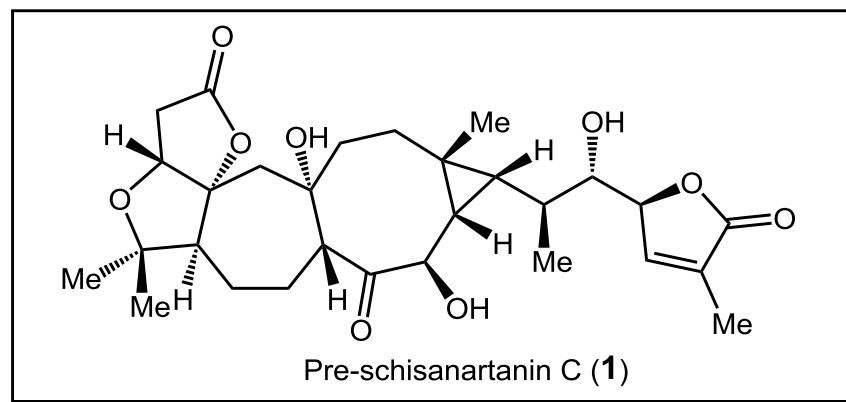
44

- 1) HF, py., then DBU (94%)
2) AD mix- α (65%)



Pre-schisanartanin C (**1**)

Summary



- 24 steps, 0.49 % overall yield;
- Gold-catalyzed intramolecular cyclopropanation of a 1,8-enyne substrate to prepare a bicyclo[6.1.0]nonane core;
- An asymmetric Diels-Alder reaction to install the initial stereogenic center;
- A regio- and stereoselective Sharpless asymmetric dihydroxylation, and a subsequent intramolecular lactonization.

The First Paragraph

Writing Strategy

Origin of Pre-schisanartanin C



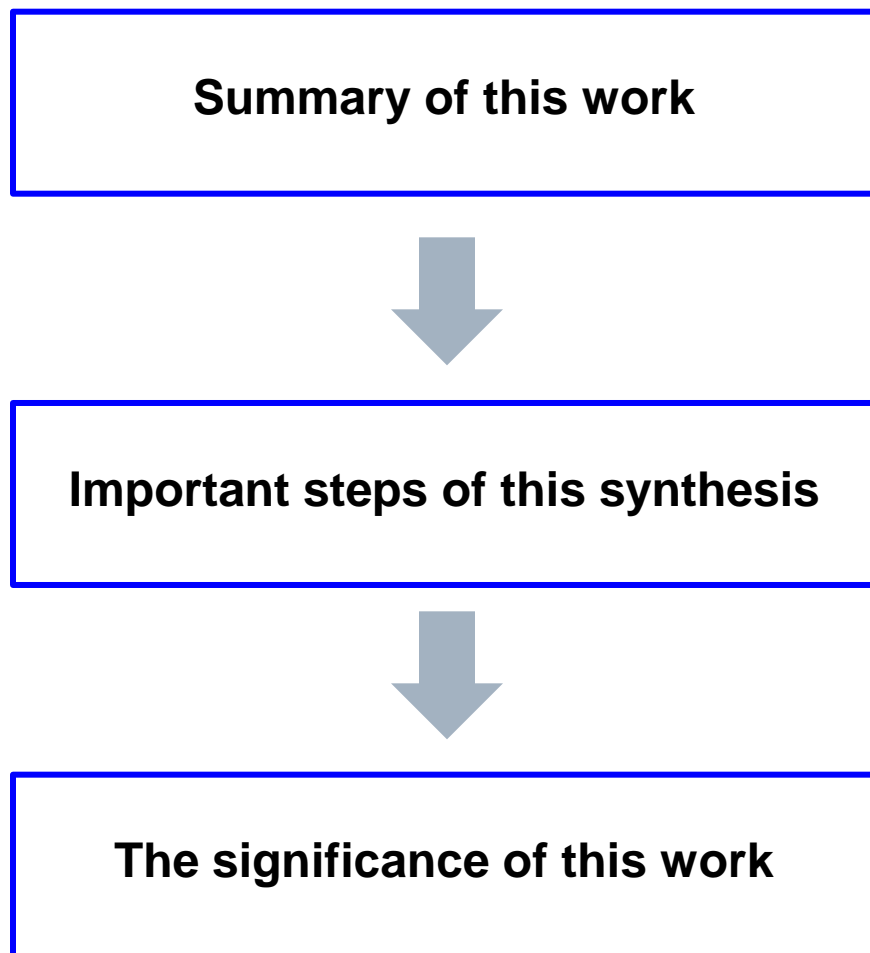
The structure and configuration

The First Paragraph

Pre-schisanartanin C, which is a typical Schisandra nortriterpenoid, was isolated from the medicinal plant Schisandra propinqua var. propinqua by Sun and coworkers in 2010. The structure and relative configuration of **1** were determined using NMR spectroscopy; however, its absolute configuration is still unknown.

The Last Paragraph

Writing Strategy



The Last Paragraph

We recently have achieved an enantioselective total synthesis of **1** in 24 steps from diene **19** with 0.49% overall yield or 1.3% overall yield based on recovered starting material. This synthesis featured (i) an asymmetric Diels-Alder reaction of diene and dienophile to install the initial stereogenic center of our target molecule, (ii) a Au-catalyzed intramolecular enyne cyclization to stereoselectively form the central bicyclo[6.1.0]nonane core, an $\text{Al}(\text{O}^t\text{Bu})_3$ -isomerization for diastereoselective installation of the crucial hydroxy ketone motif, and (iii) a Sharpless asymmetric dihydroxylation for regio- and stereoselective installation of the stereogenic centers. The developed chemistry lays a foundation for a planned access to the total syntheses of other family members bearing highly rigid bicyclo[6.1.0]-nonane cores.

Representative Examples

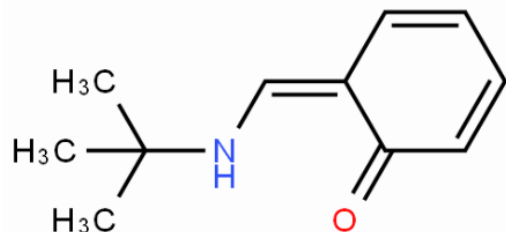
The structure and relative configuration of **1** **were determined using** NMR spectroscopy. (对测定方法的描述)

This synthesis featured (i) an asymmetric Diels-Alder reaction of diene and dienophile to **install the initial stereogenic center of** our target molecule. (构建立体中心的描述)

The developed chemistry **lays a foundation for** a planned access to the total syntheses of other family members bearing highly rigid bicyclo[6.1.0]-nonane cores. (奠定基础的描述)

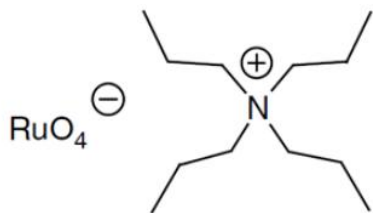
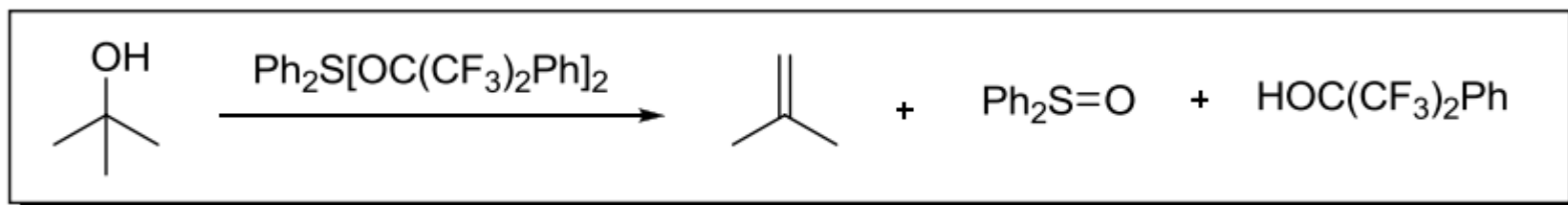
Acknowledgement

***Thanks
for your attention***



(6Z)-6-[(tert-butylamino)methylidene]cyclohexa-2,4-dien-1-one, $\text{Cu}(\text{TBS})_2$

Tris(2,6-dimethyl-3,5-heptanedionato)iron(III), $\text{Fe}(\text{dibm})_3$



Tetra-*n*-propylammonium perruthenate

