

Literature Report 1

Total Syntheses of Polycyclic Diterpenes Phomopsene, Methyl Phomopsenonate, and *iso*-Phomopsene

Reporter: Kai Xue

Checker: Jian Chen

Yin, J.-J.; Wang, Y.-P.; Tu, Y.-Q. *J. Am. Chem. Soc.* **2023**, *145*, 21170

2023-10-23

CV of Prof. Yong-Qiang Tu

Background:

- **1985-1989** Ph.D., Lanzhou University
- **1993-1995** Postdoc., University of Queensland
- **1995-2014** Professor, Lanzhou University
- **2014-** Professor, Lanzhou University and Shanghai Jiao Tong University



Research:

- Organic Synthetic Methodology
- Total Synthesis of Natural Products
- Organometallic Chemistry

Contents

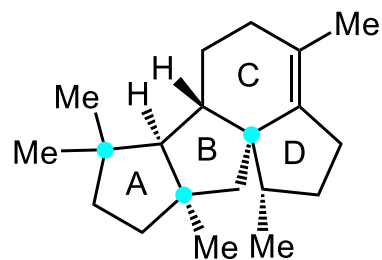
1 Introduction

2 Retrosynthetic Analysis

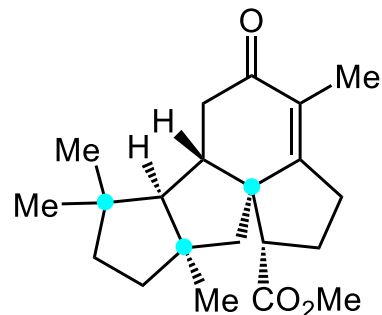
3 Total Synthesis of Diterpenes Phomopsene

4 Summary

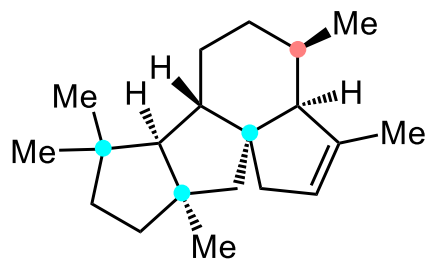
Introduction



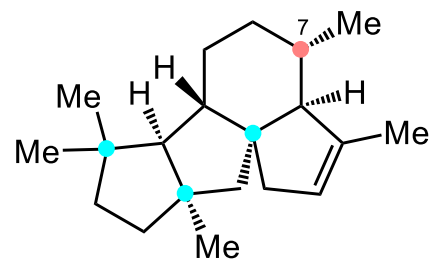
Phomopsene (1)



Methyl Phomopsenonate (2)



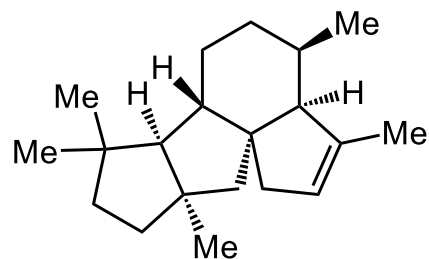
***iso*-Phomopsene (3a)**



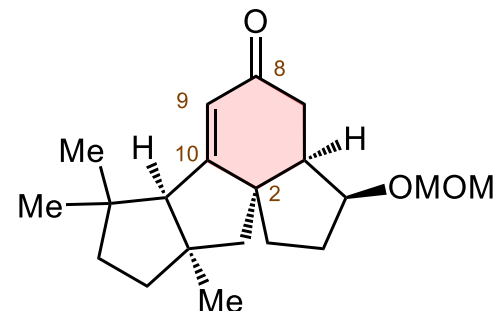
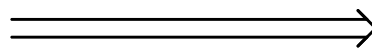
***iso*-Phomopsene (3)**

- The phomopsene diterpenes were isolated from the fermentation of fungi
- A linear fused 5/5/6-tricyclic ring system (A–C) with an angularly fused cyclopentane ring (D)
- Consecutive stereocenters, highly congested quaternary carbon centers

Retrosynthetic Analysis

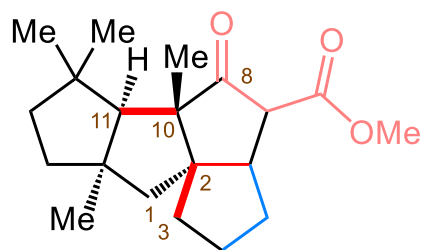


iso-Phomopsene (3a)

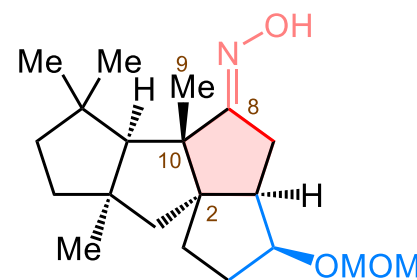
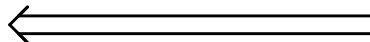


4

(5/5/6/5 tetracycle)



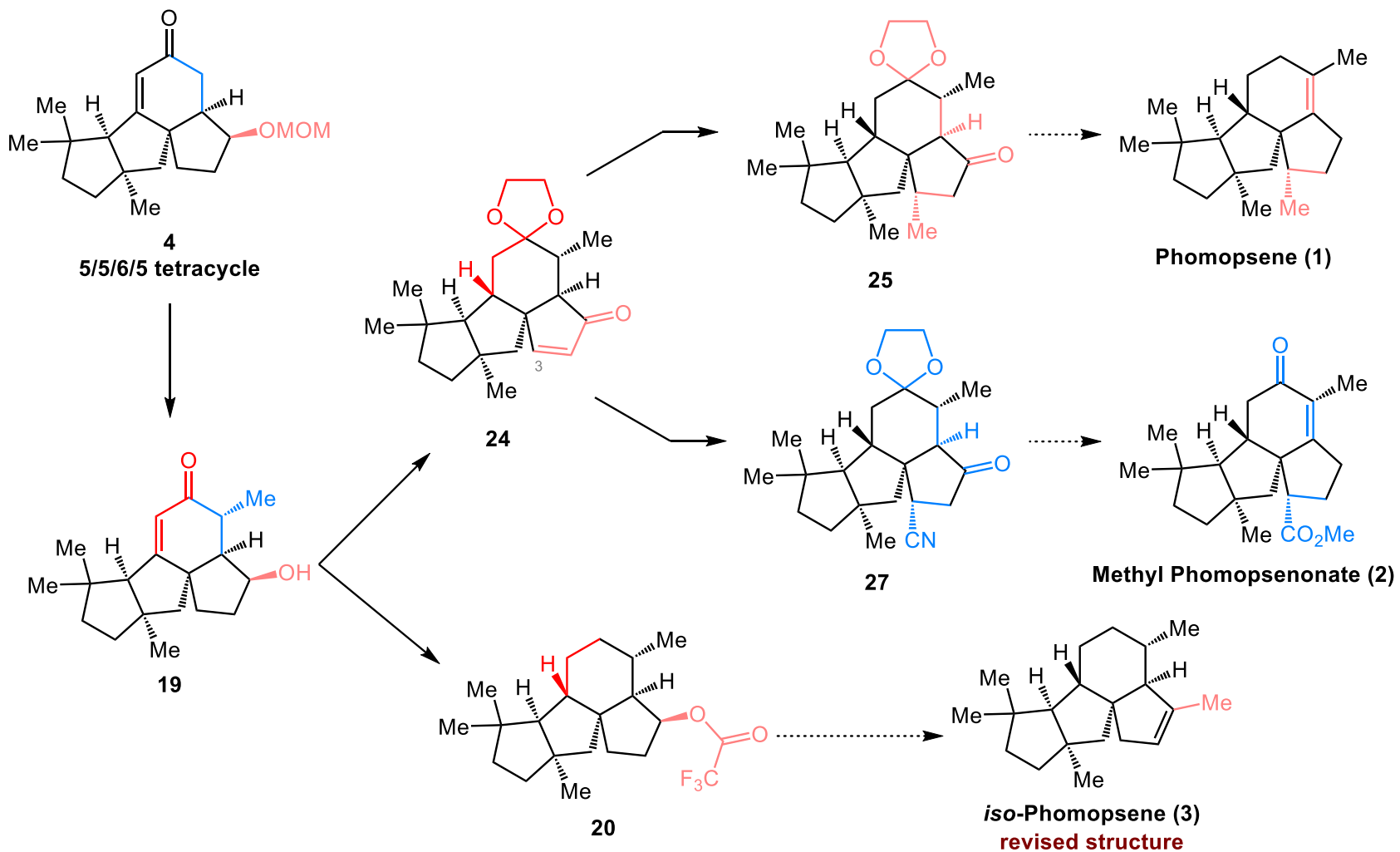
6



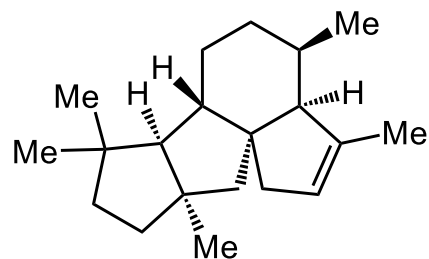
5

(5/5/5/5 tetracycle)

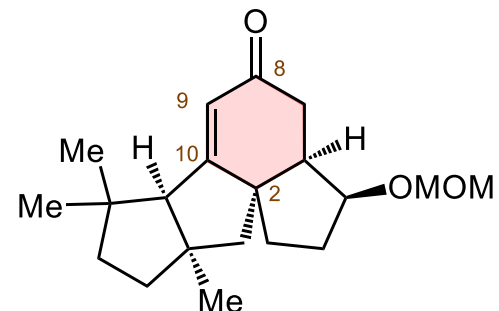
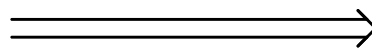
Retrosynthetic Analysis



Retrosynthetic Analysis



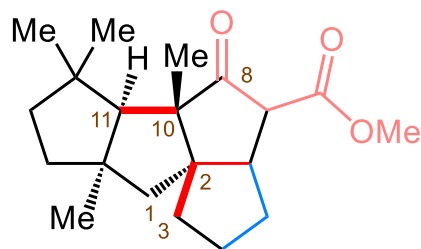
iso-Phomopsene (3a)



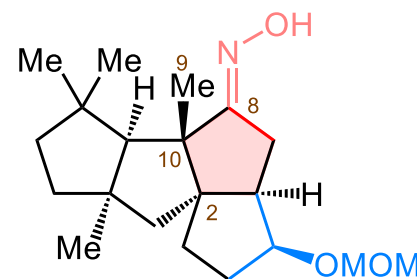
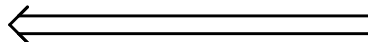
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(5/5/6/5 tetracycle)

*unusual
fragmentation/
reconstruction*



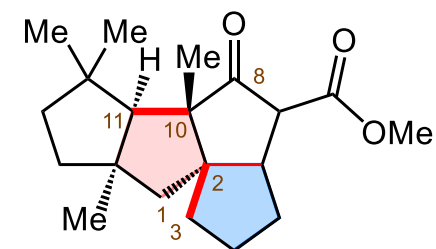
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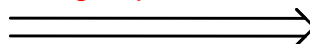
(5/5/5/5 tetracycle)

Retrosynthetic Analysis

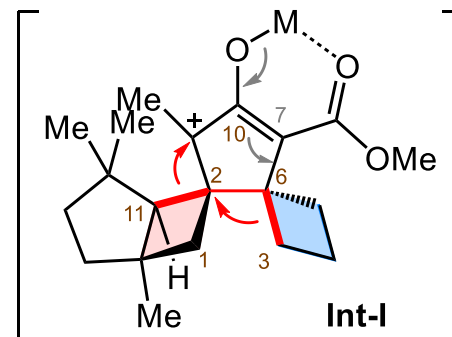


6

*stereospecific
cascade
ring expansions*

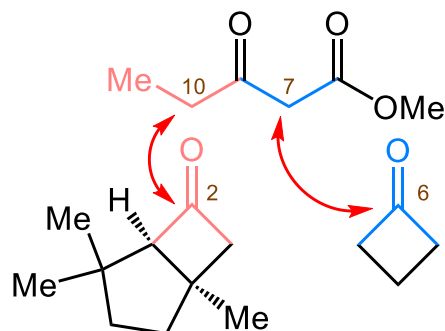
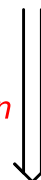


anti-periplanar C-C bond 1,2-shifts



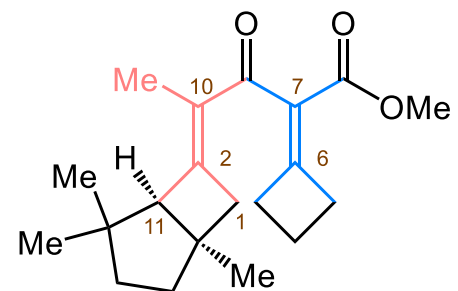
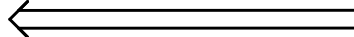
Int-I

*Nazarov
cyclization*



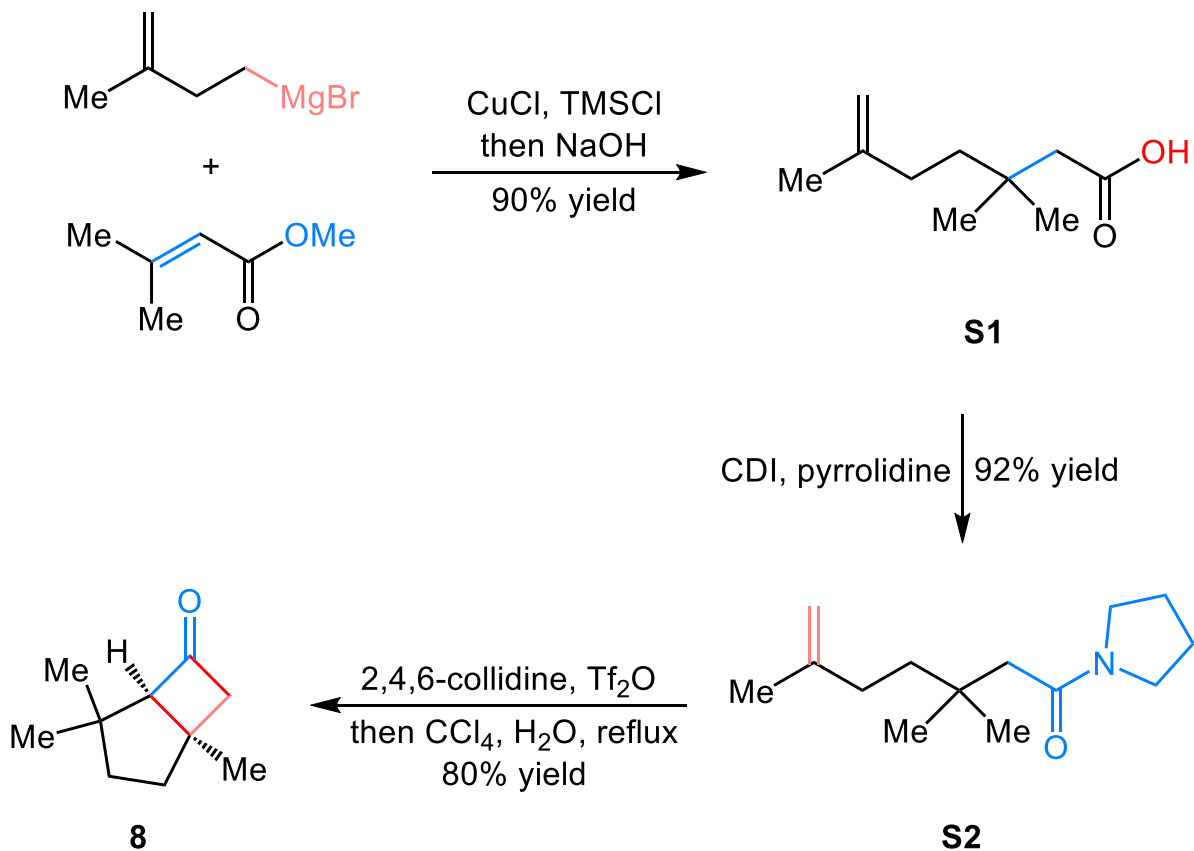
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Aldol condensation

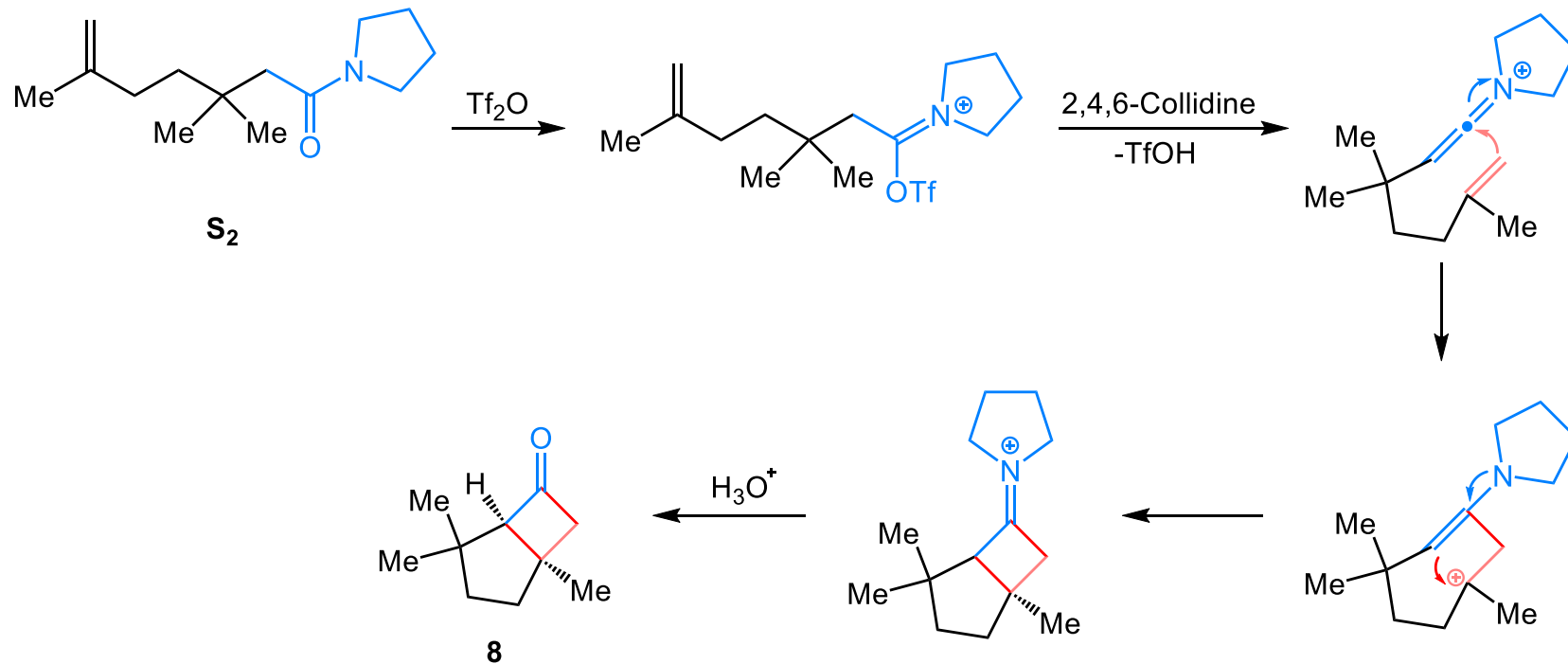


7

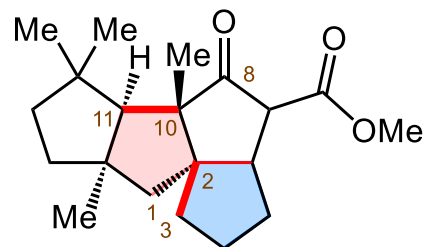
Stage 1: Synthesis of Compound 8



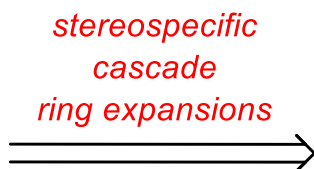
Stage 1: Synthesis of Compound 8



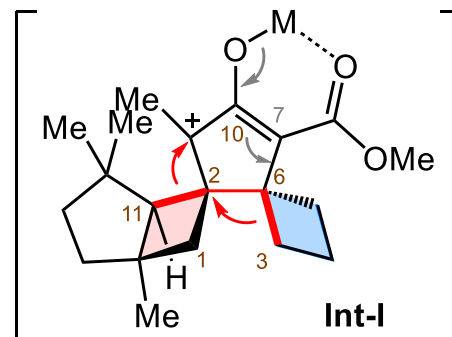
Stage 2: Synthesis of Tertacyclic Ring Compound 6



6

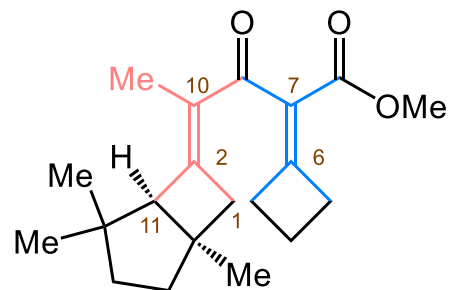


anti-periplanar C-C bond 1,2-shifts

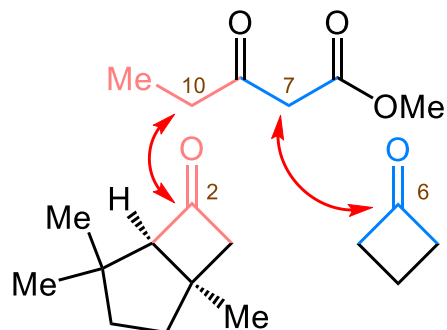


Int-I

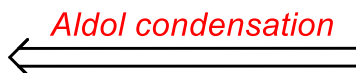
*Nazarov
cyclization*



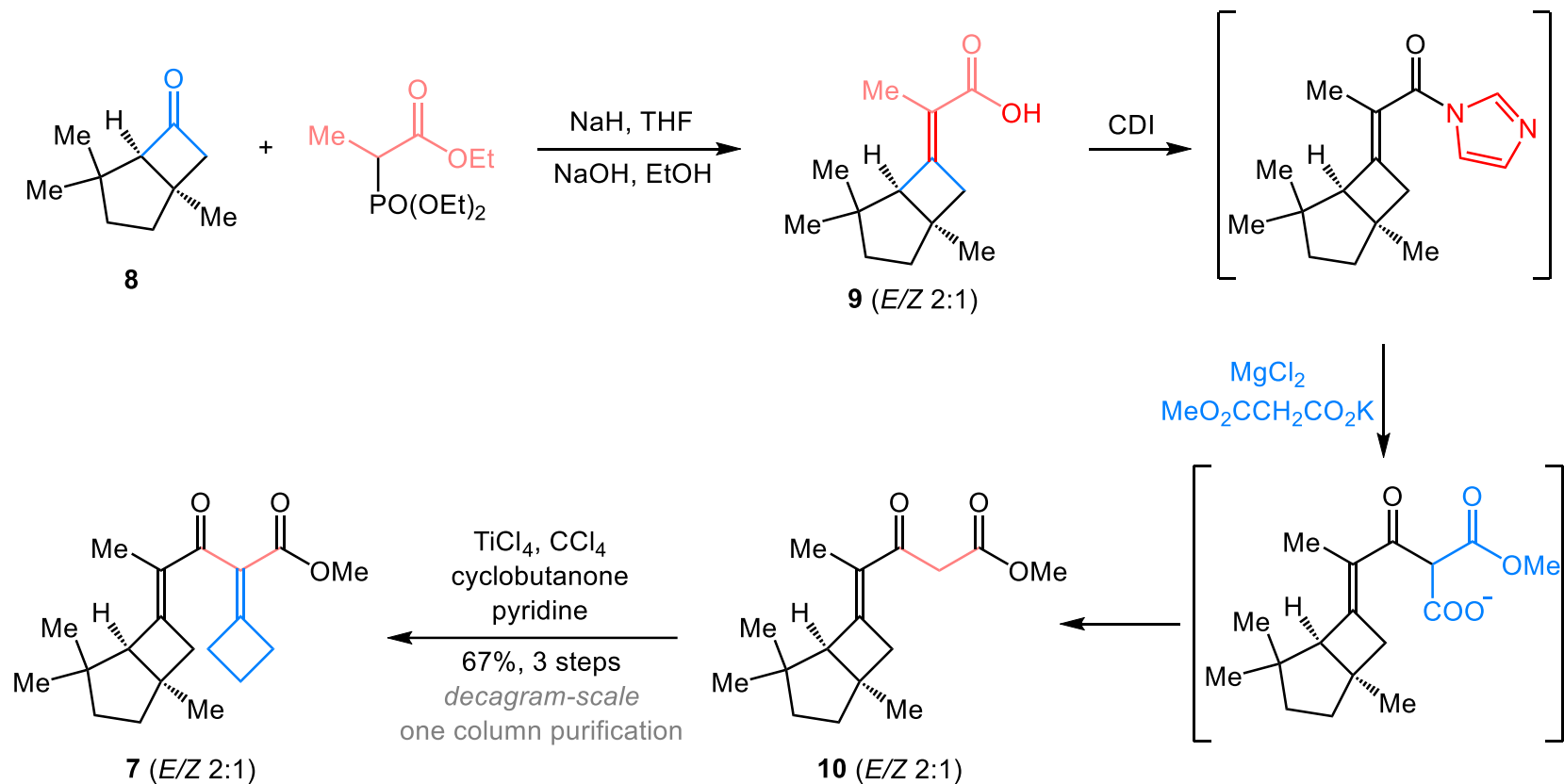
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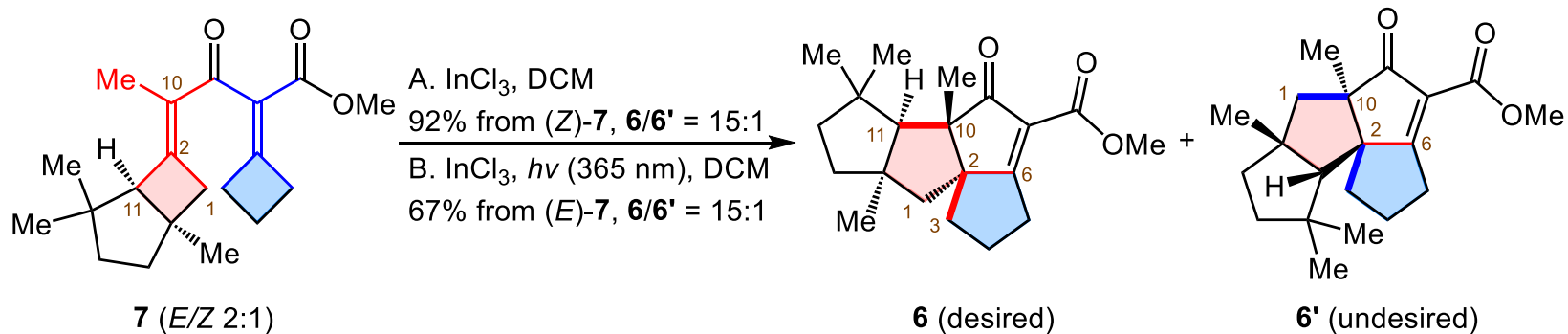
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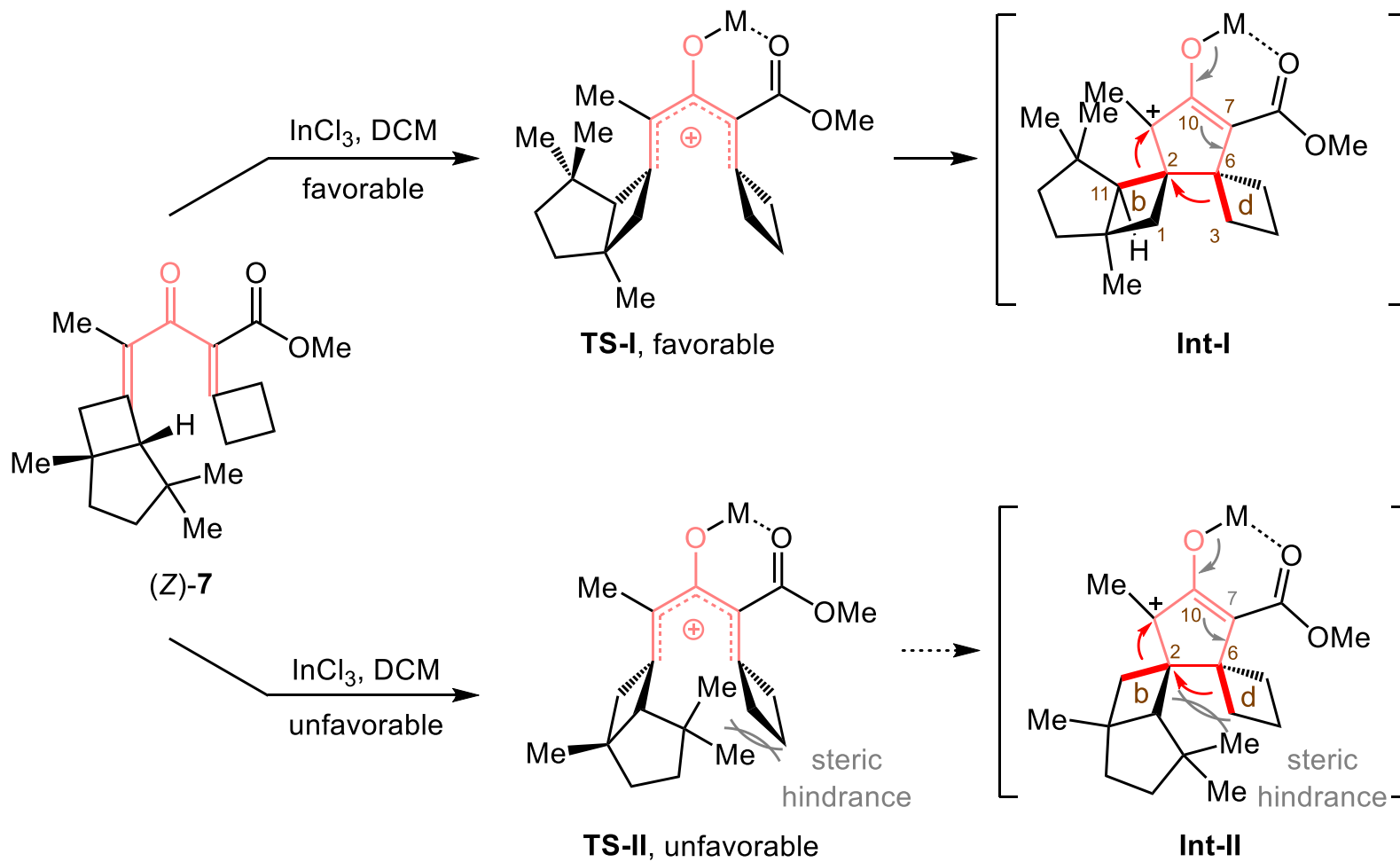
Stage 2: Synthesis of Tertacyclic Ring Compound 6



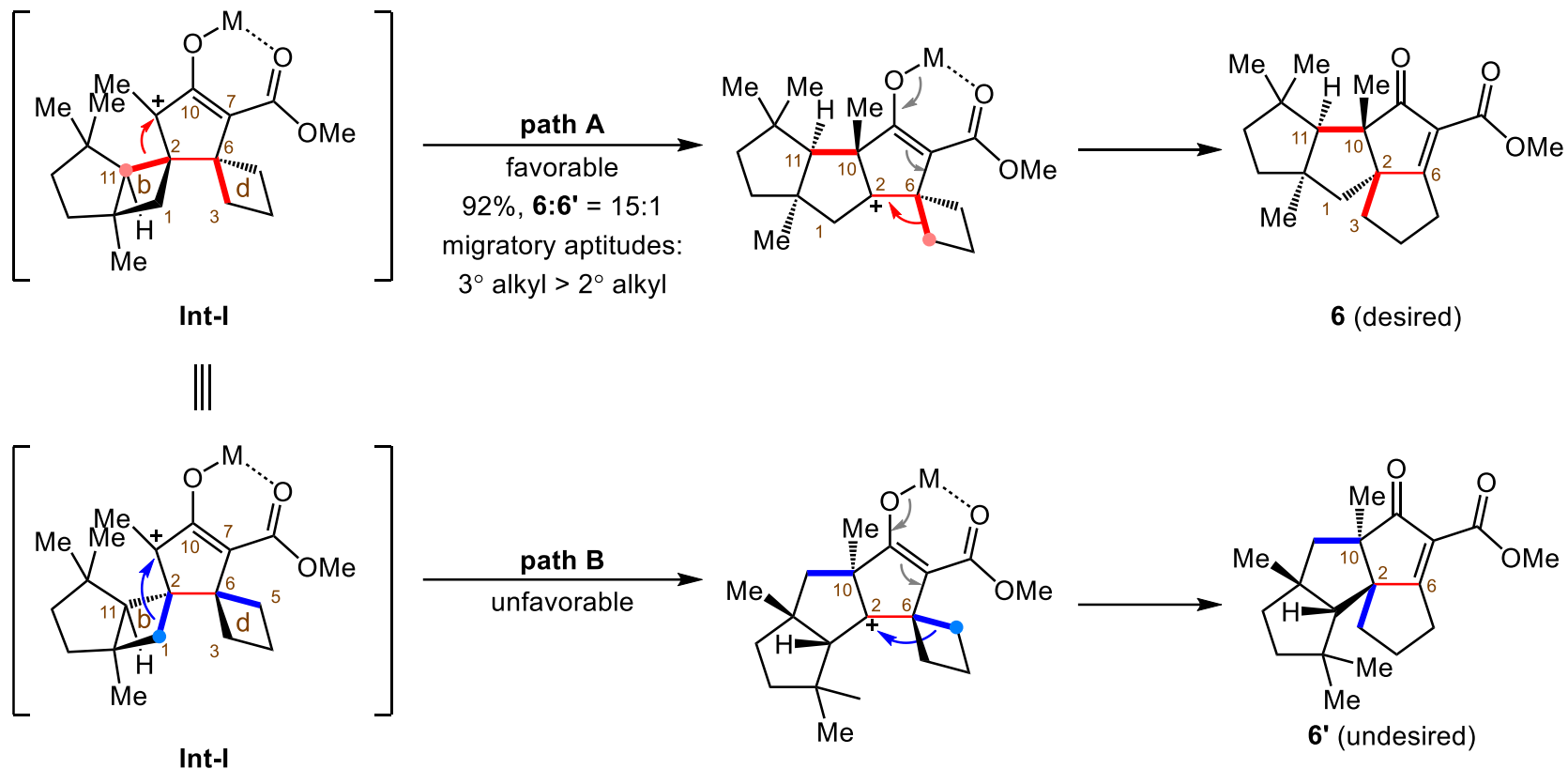
Nazarov Cyclization/Double Ring Expansions



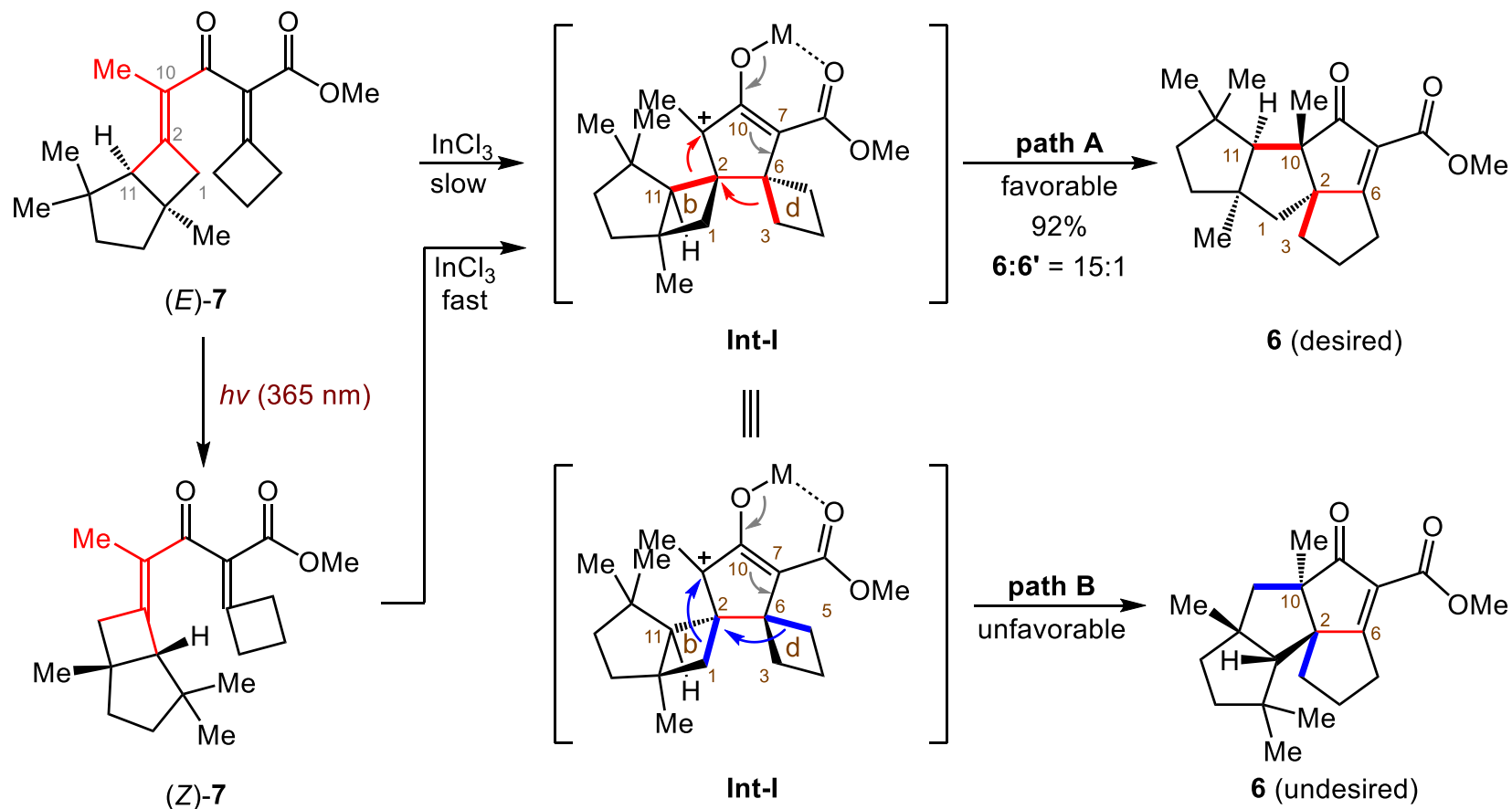
Nazarov Cyclization/Double Ring Expansions



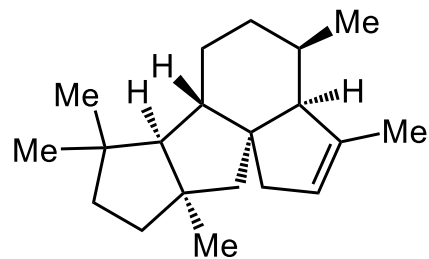
Nazarov Cyclization/Double Ring Expansions



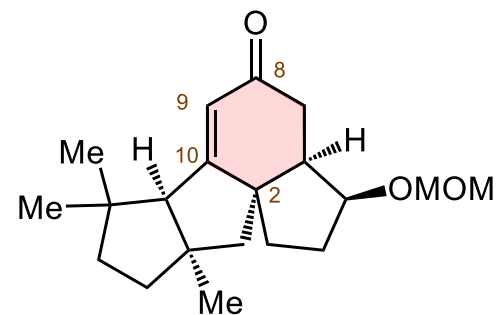
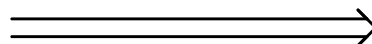
Nazarov Cyclization/Double Ring Expansions



Stage 3: Synthesis of Key Intermediate 4



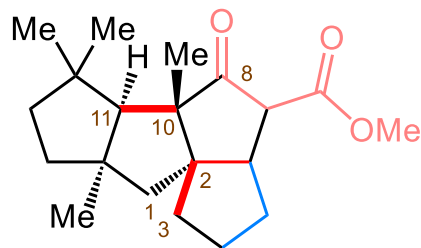
iso-Phomopsene (3a)



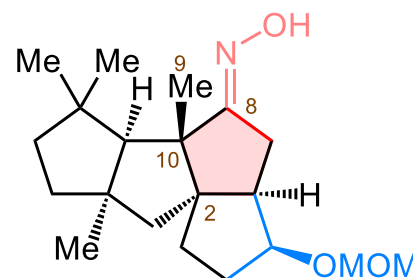
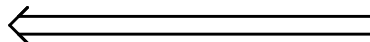
4

(5/5/6/5 tetracycle)

*unusual
fragmentation/
reconstruction*



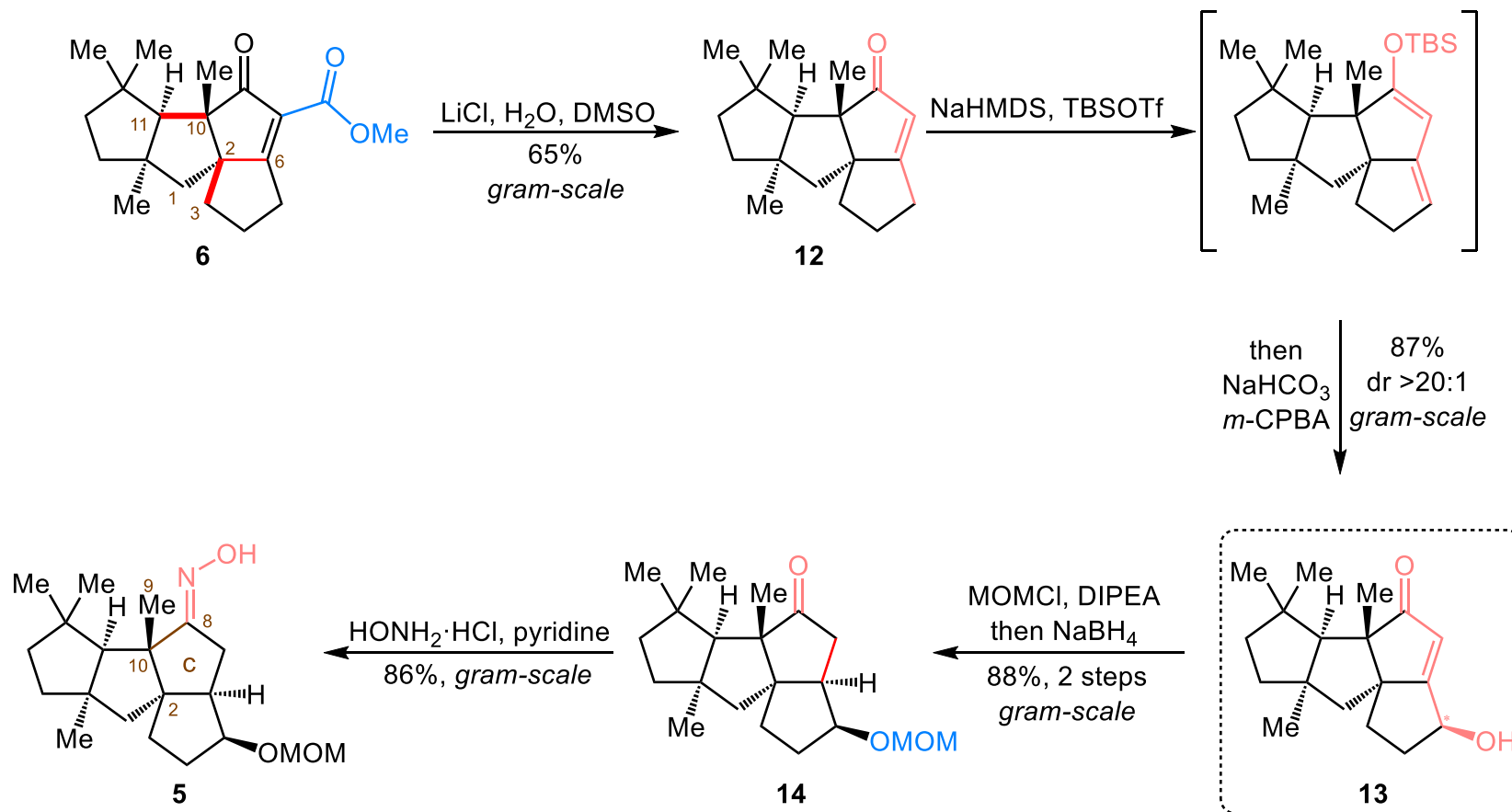
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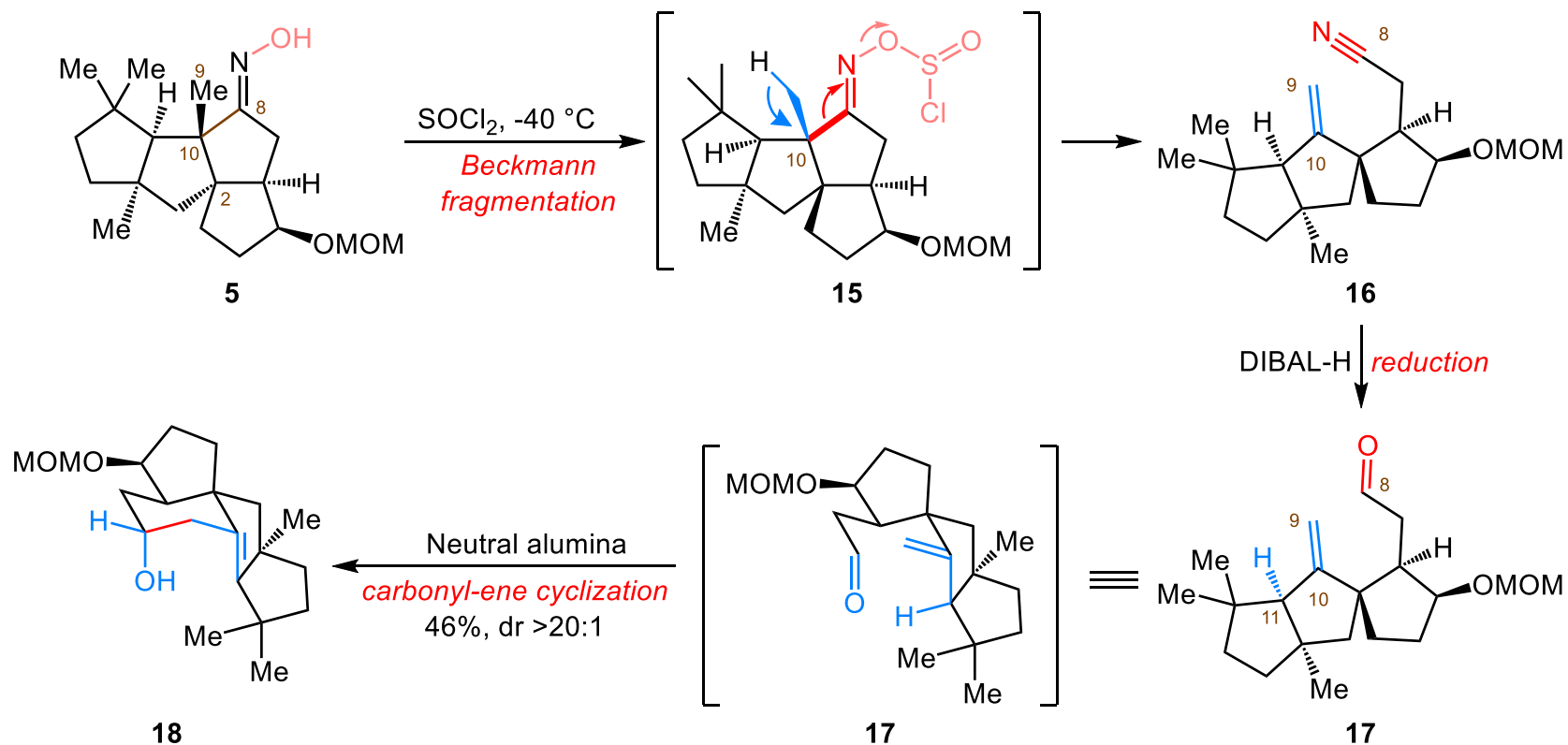
5

(5/5/5/5 tetracycle)

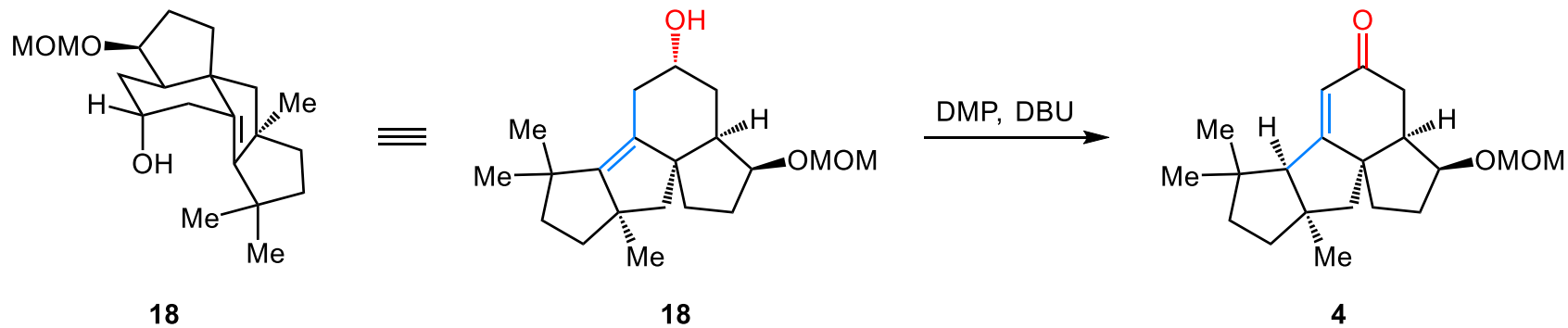
Stage 3: Synthesis of Key Intermediate 4



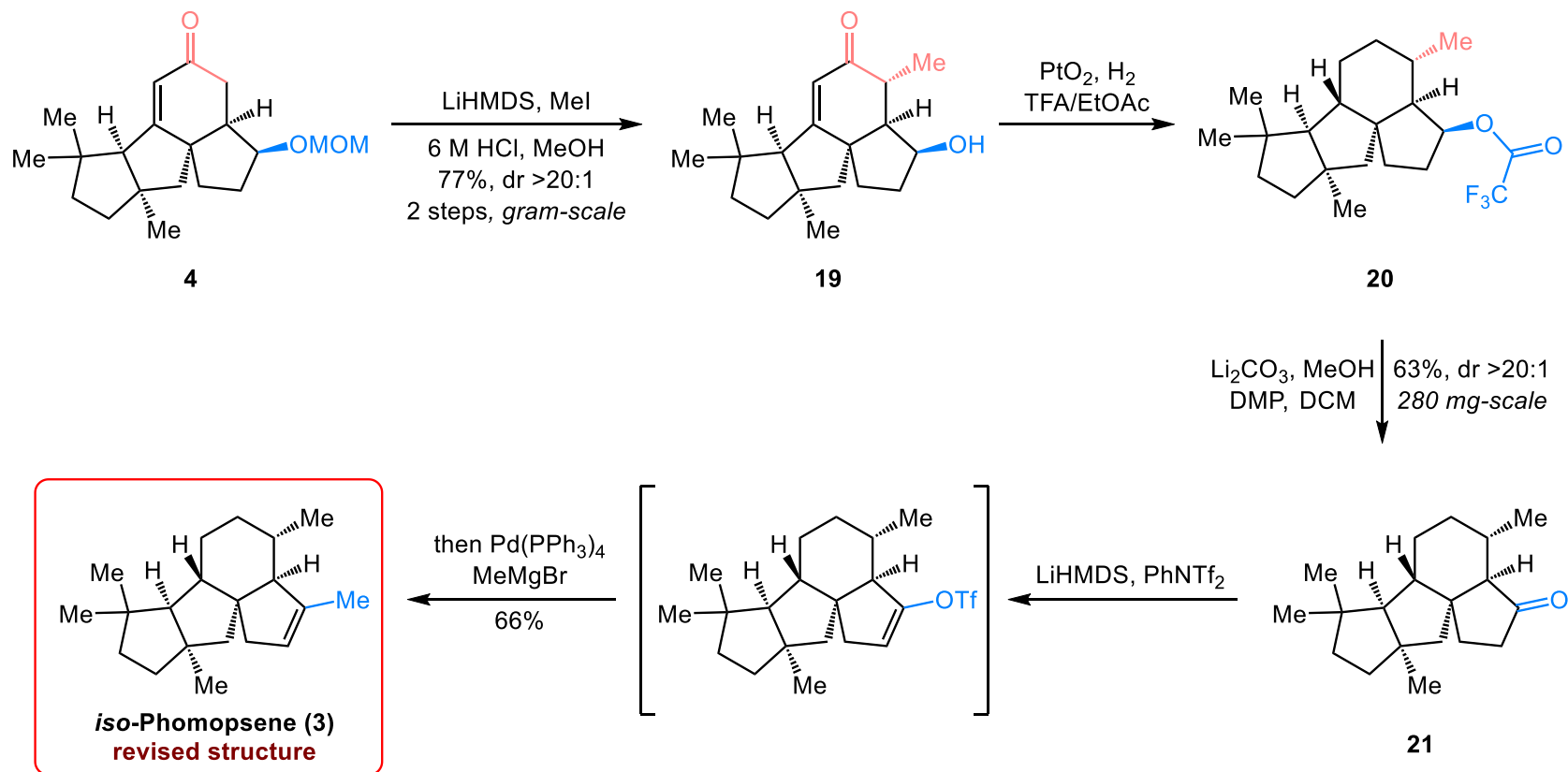
Stage 3: Synthesis of Key Intermediate 4



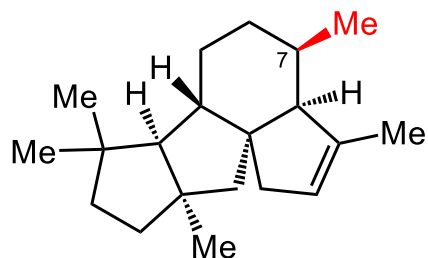
Stage 3: Synthesis of Key Intermediate 4



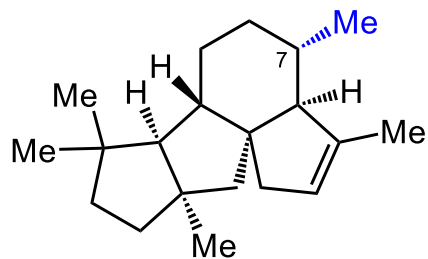
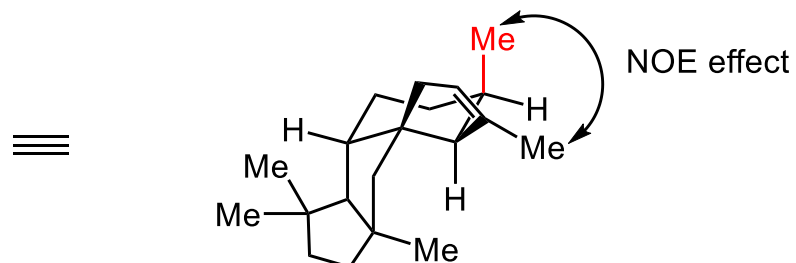
Stage 4: Synthesis of *iso*-Phomopsene



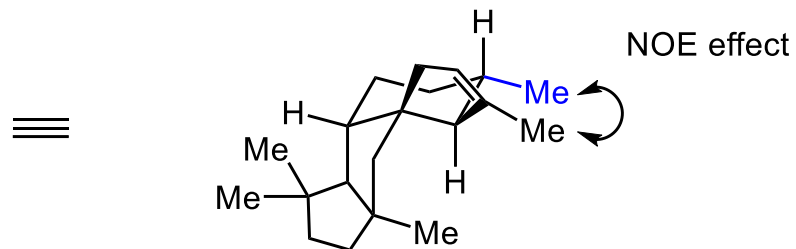
Stage 4: Synthesis of Target Molecules



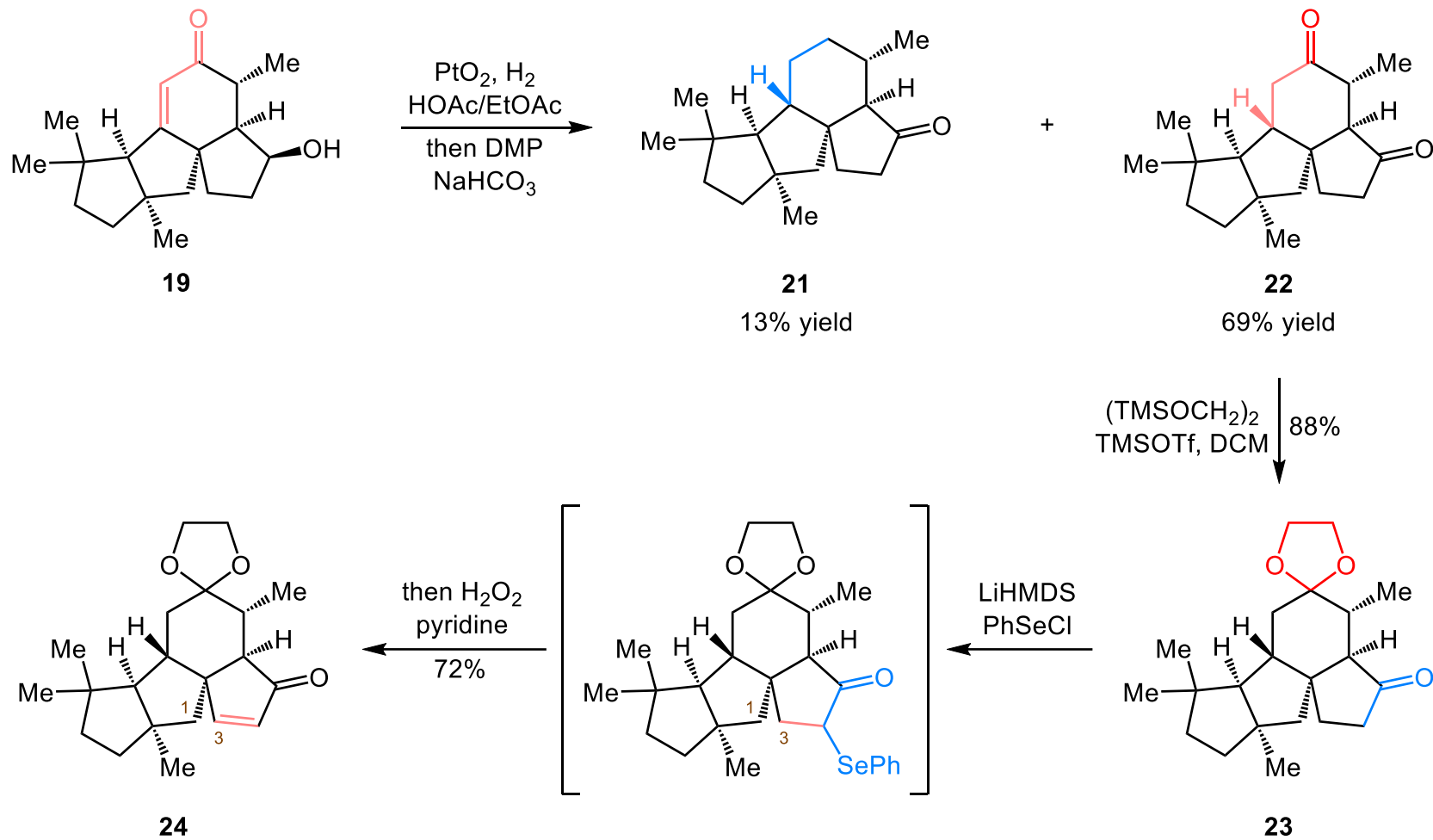
iso-Phomopsene (3a)



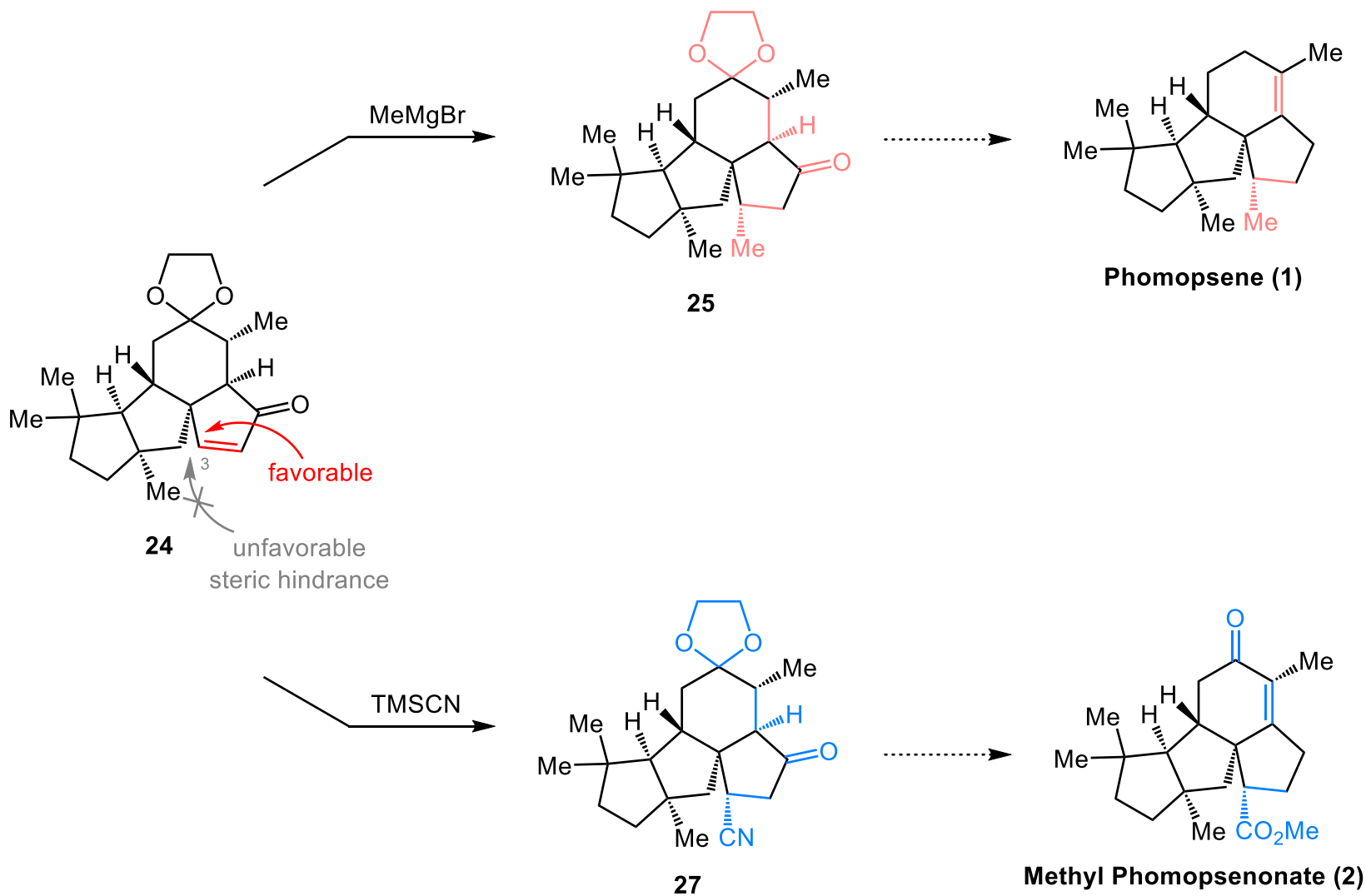
iso-Phomopsene (3)
revised structure



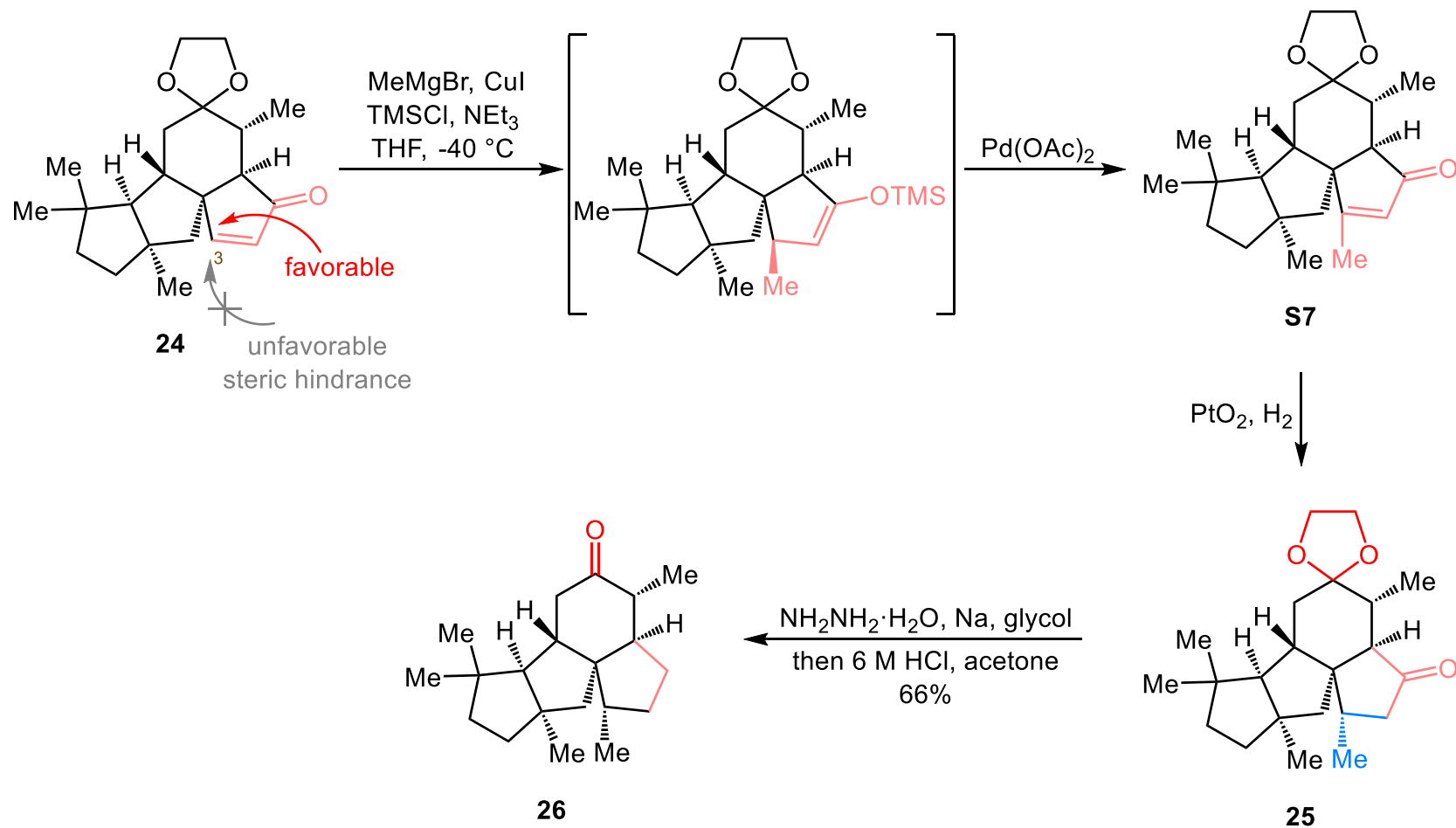
Stage 4: Synthesis of Compound 1 and 2



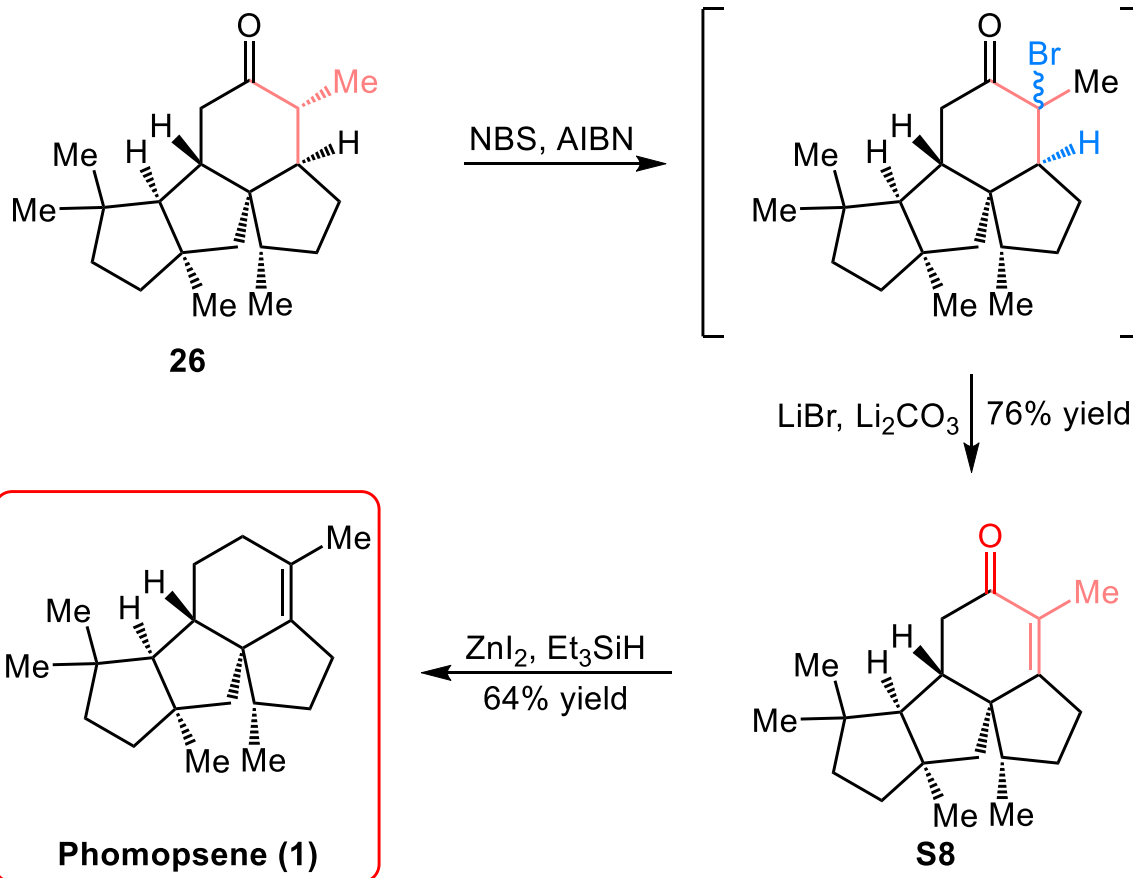
Stage 4: Synthesis of Compound 1 and 2



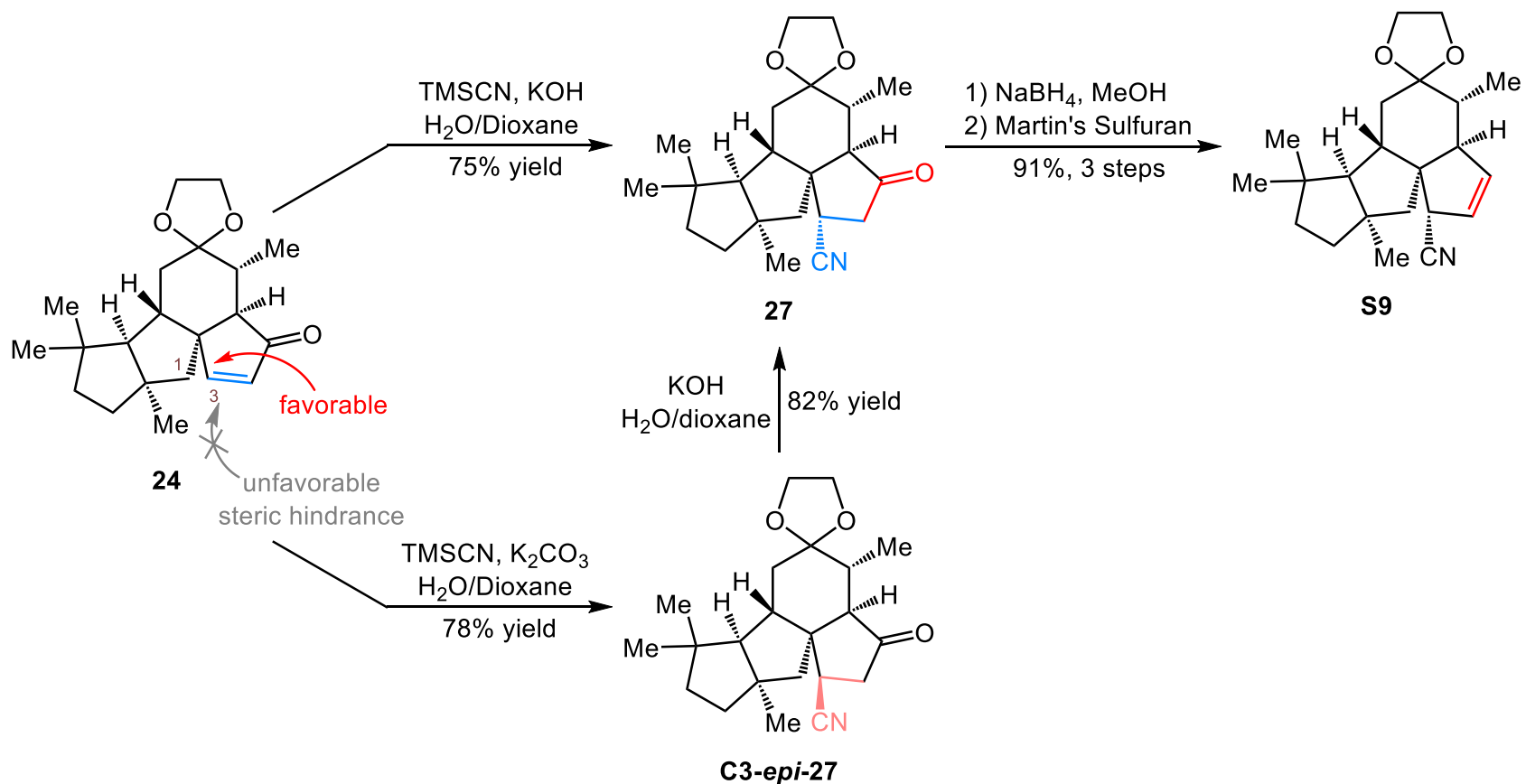
Stage 4: Synthesis of Phomopsene



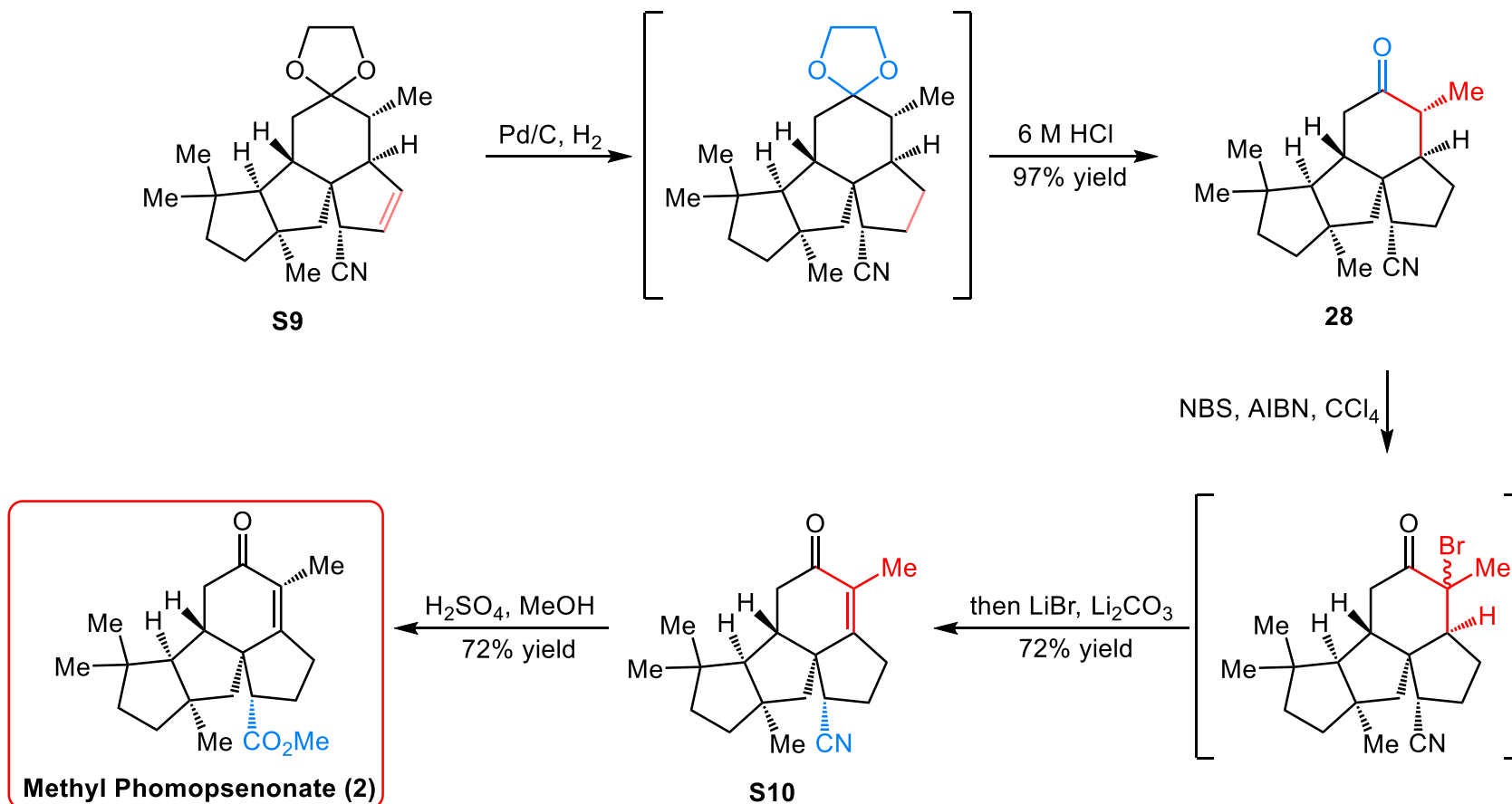
Stage 4: Synthesis of Phomopsene



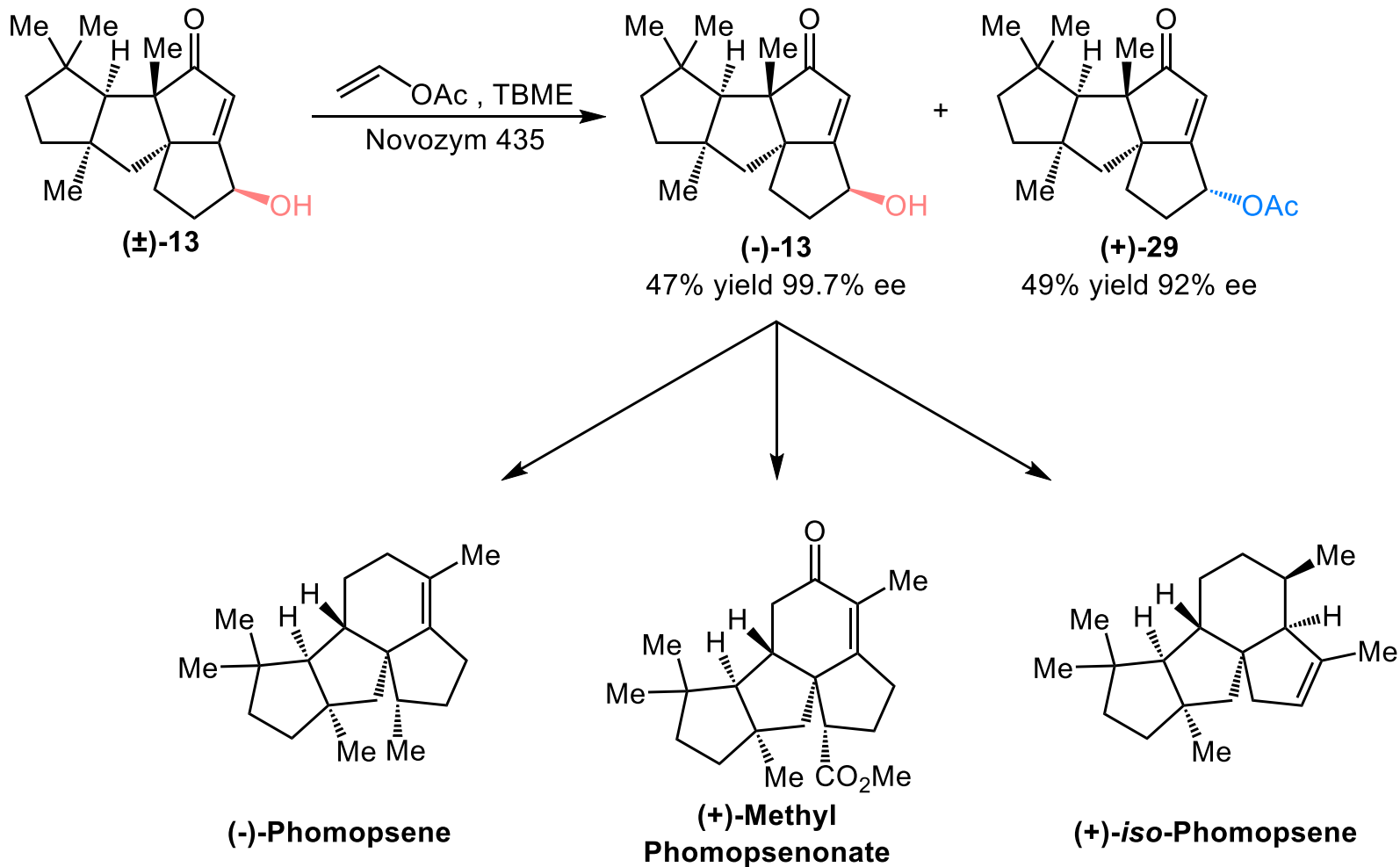
Stage 4: Synthesis of Methyl Phomopsenonate



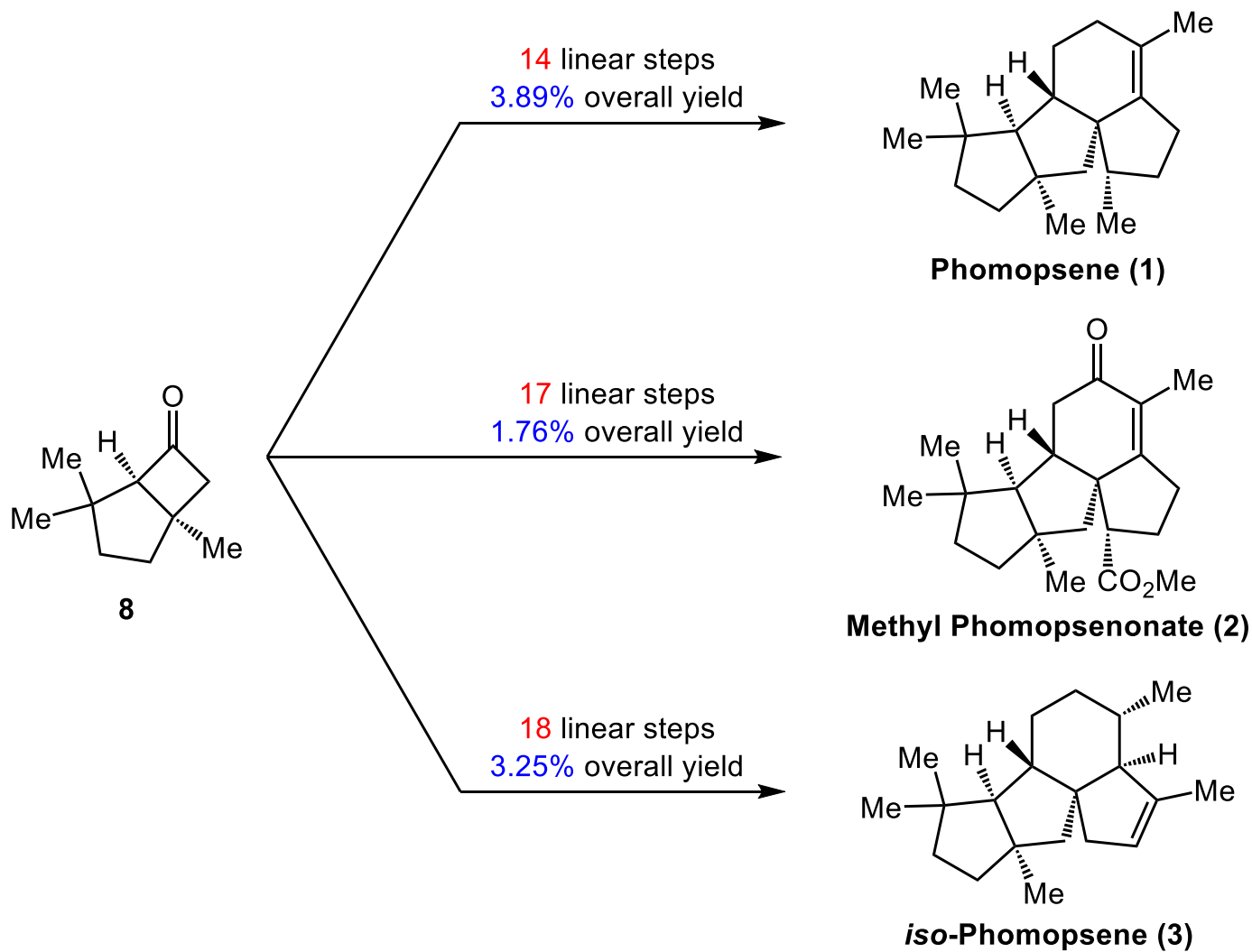
Stage 4: Synthesis of Methyl Phomopsenonate



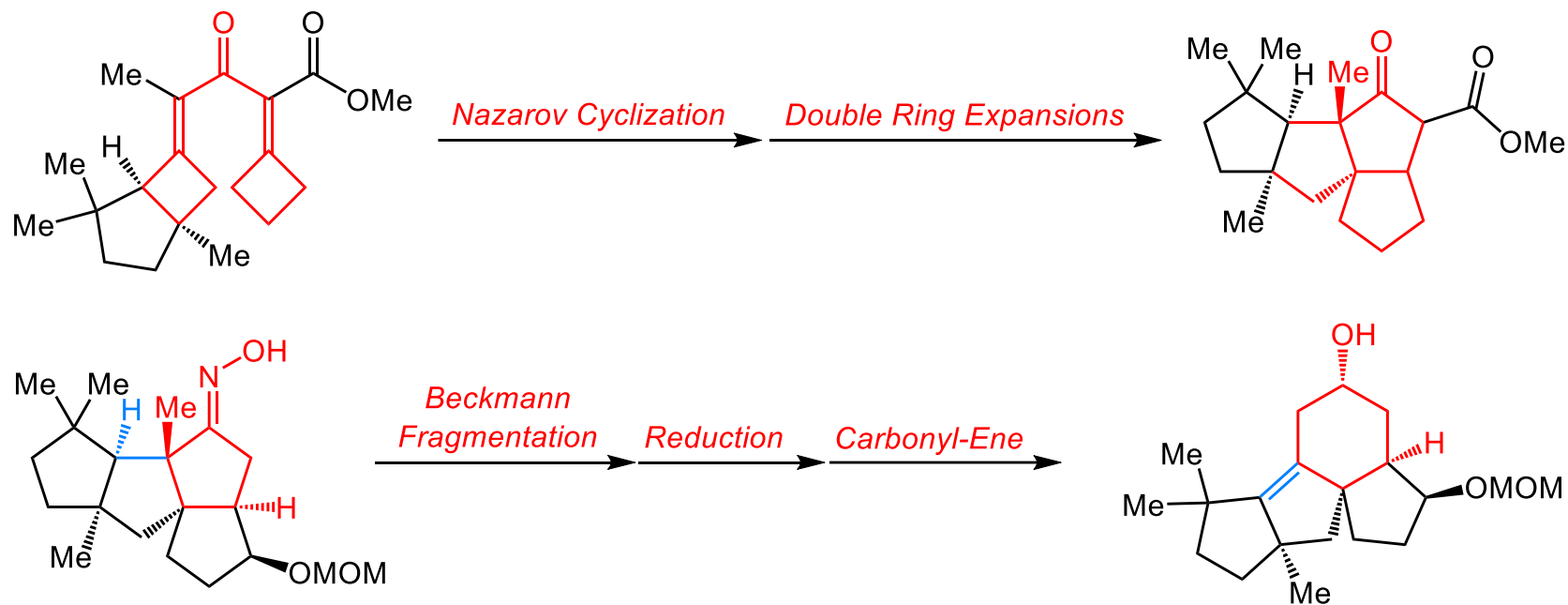
Enantioselective Syntheses



Summary



Summary

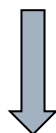


- Tandem Nazarov cyclization/double ring expansions
- A one-pot Beckmann fragmentation/reduction/carbonyl-ene protocol

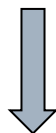
The First Paragraph

写作思路

碳碳键重组在复杂天然分子仿生合成中的重要作用



构建包含高应变桥接、螺环和并环的骨架

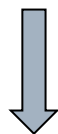


串联纳扎罗夫环化/双环扩张反应

The Last Paragraph

写作思路

对本文的工作进行总结



展望串联纳扎罗夫环化/双环扩张反应的应用

Representative Examples

- This strategy has **continuously stimulated** (激励着) synthetic chemists to develop synthetically useful rearrangement reactions, such as..., with the aim of achieving rapid and efficient synthesis of...
- **Despite significant advancements** in this field, it is still highly **desirable** to develop more powerful and versatile synthetic methods for the reorganization of C–C single bonds. (尽管有很大的进展, 但是仍有…的动力)
- Our synthesis employed..., including the tandem Nazarov cyclization and ... **protocol** (方案) to efficient construction of the requisite...skeleton of target molecules.

Acknowledgement

Thanks for Your Attention