

Literature Report 2

Concise Synthesis of Norzoanthamine Enabled by a Set of Photochemical Transformations

Reporter: Xin-Yu Zhan
Checker: Yu-Yang Shi

Sun, Y.; Zhang, X.; Jiang, F.; Zhang, M.; Wu, W.; Sun, Y. *J. Am. Chem. Soc.* **2024**, *146*, 32305

2025-04-07

CV of Prof. Yu Sun(孙域)



Background:

- ❑ 2007-2011 B.S., Fudan University
- ❑ 2011-2016 Ph.D., Shanghai Institute of Organic Chemistry
- ❑ 2016-2017 Assistant Researcher, Shanghai Institute of Organic Chemistry
- ❑ 2017-2020 Postdoctoral fellow, Boston College
- ❑ 2020-now Tenure-track, Fudan University

Research:

- Total Synthesis of Bioactive Natural Products
- Structure-activity Relationship of Natural Products
- Development of New Reactions

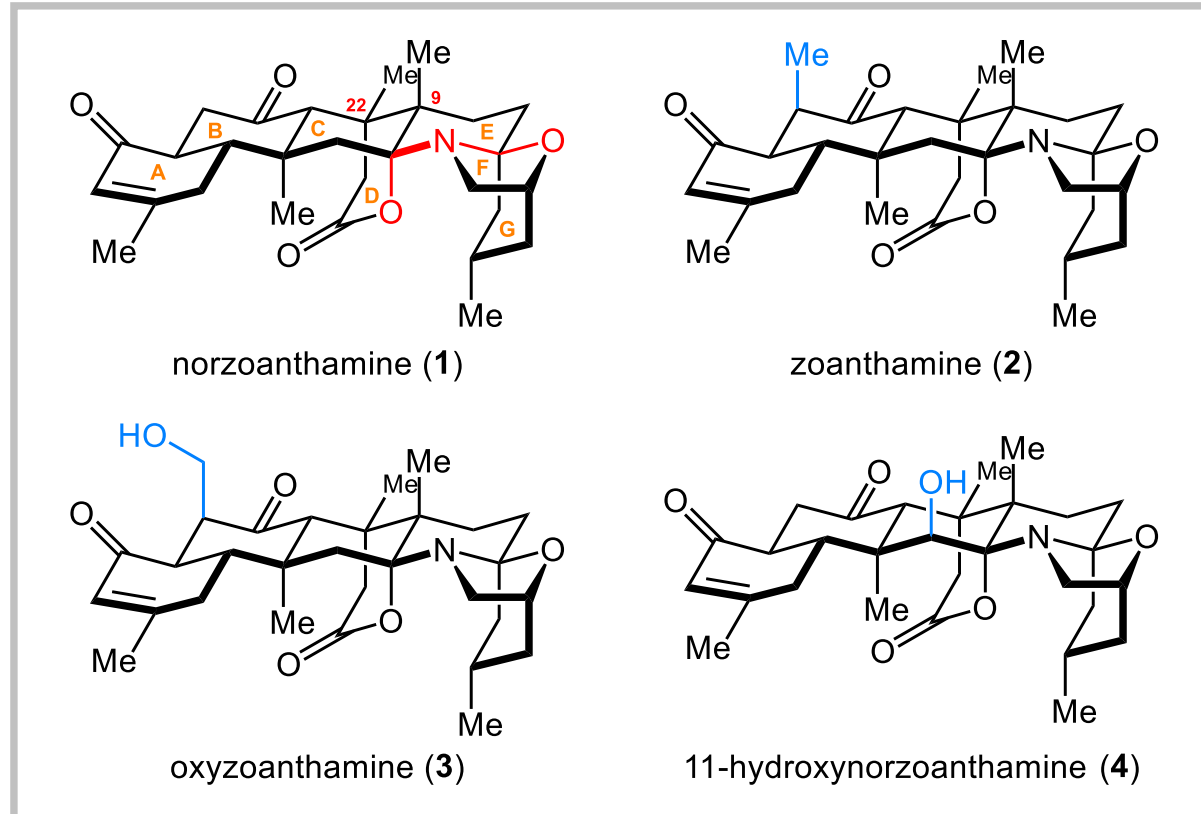
Contents

1 Introduction

2 Total Syntheses of Norzoanthamine

3 Summary

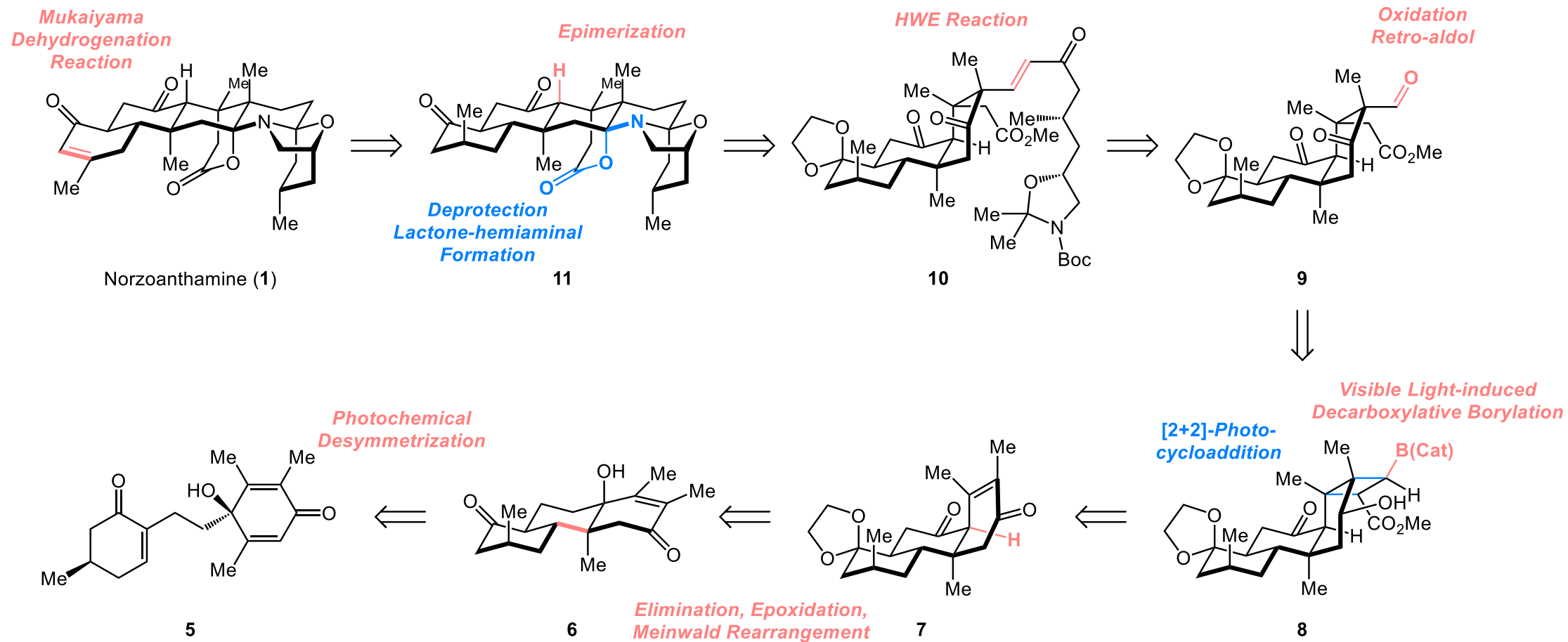
Introduction



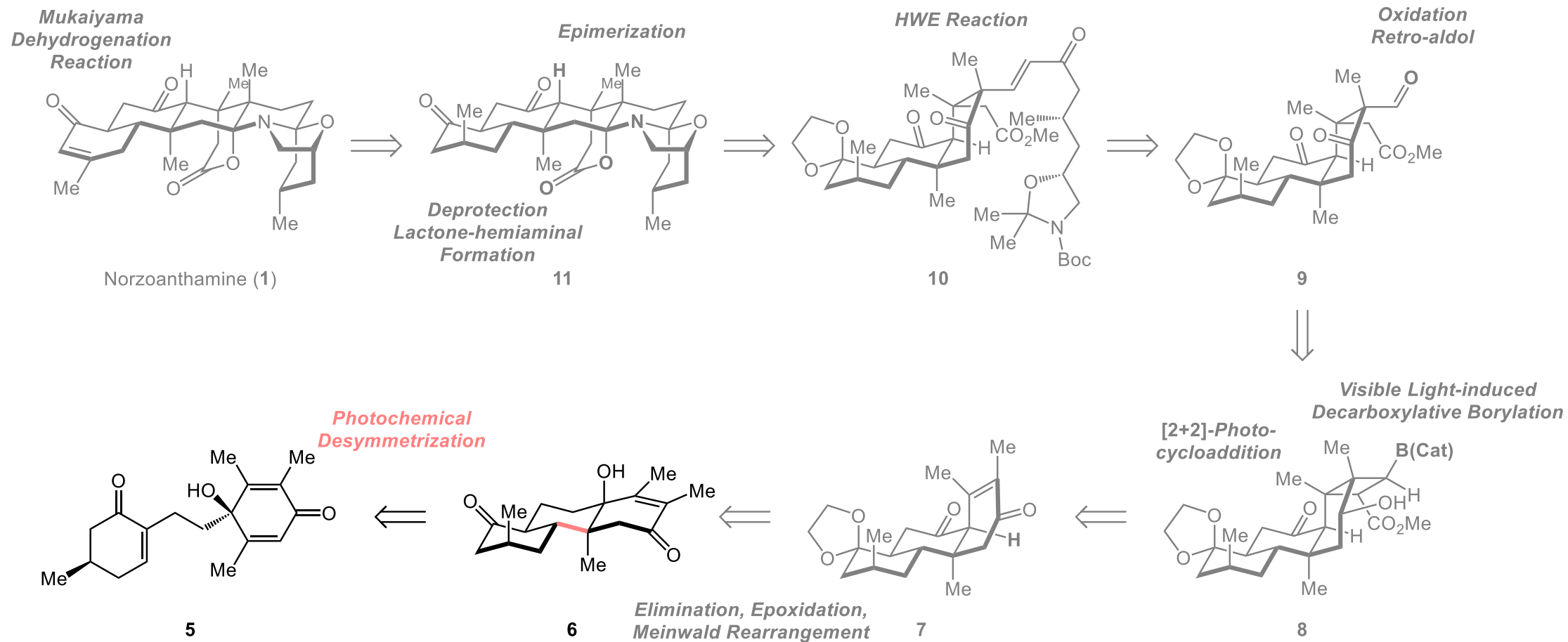
Zoanthus

- Vicinal All-carbon Quaternary Stereogenic Centers
- Anti-osteoporosis; Anti-tumor; Anti-inflammation; Neuroprotective Bioactivity

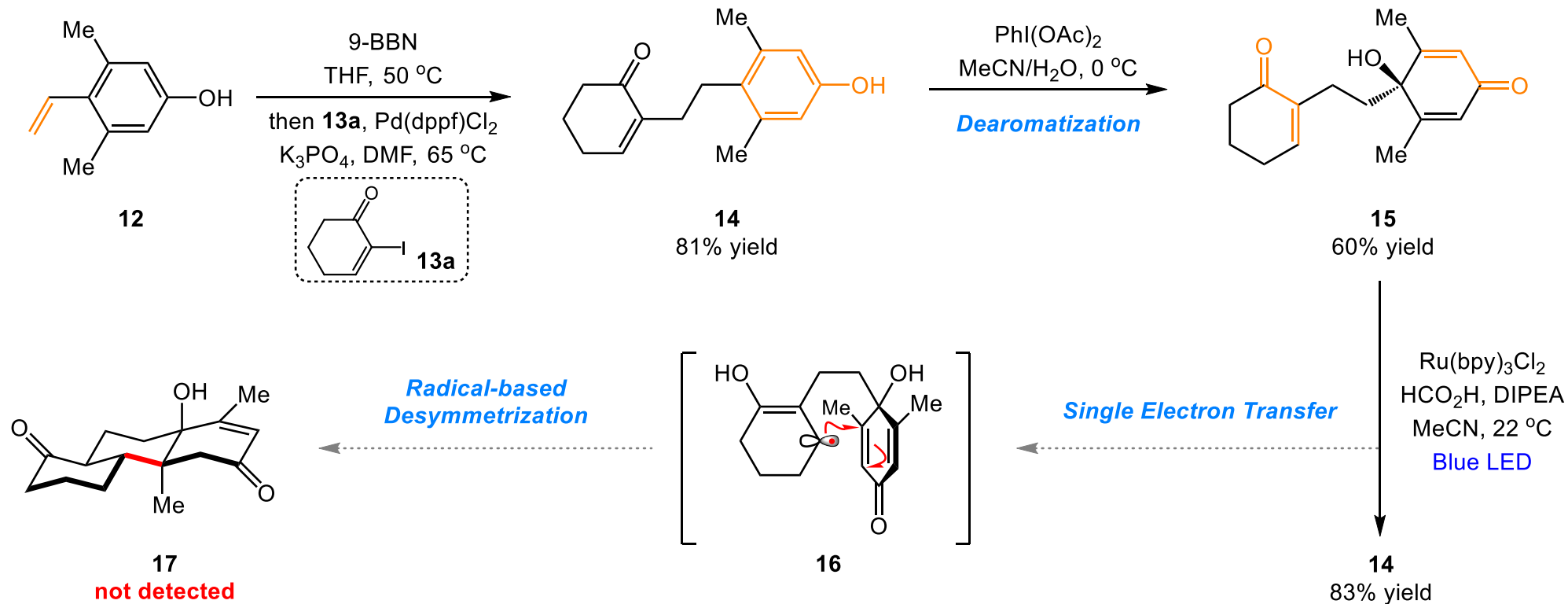
Retrosynthetic Analysis



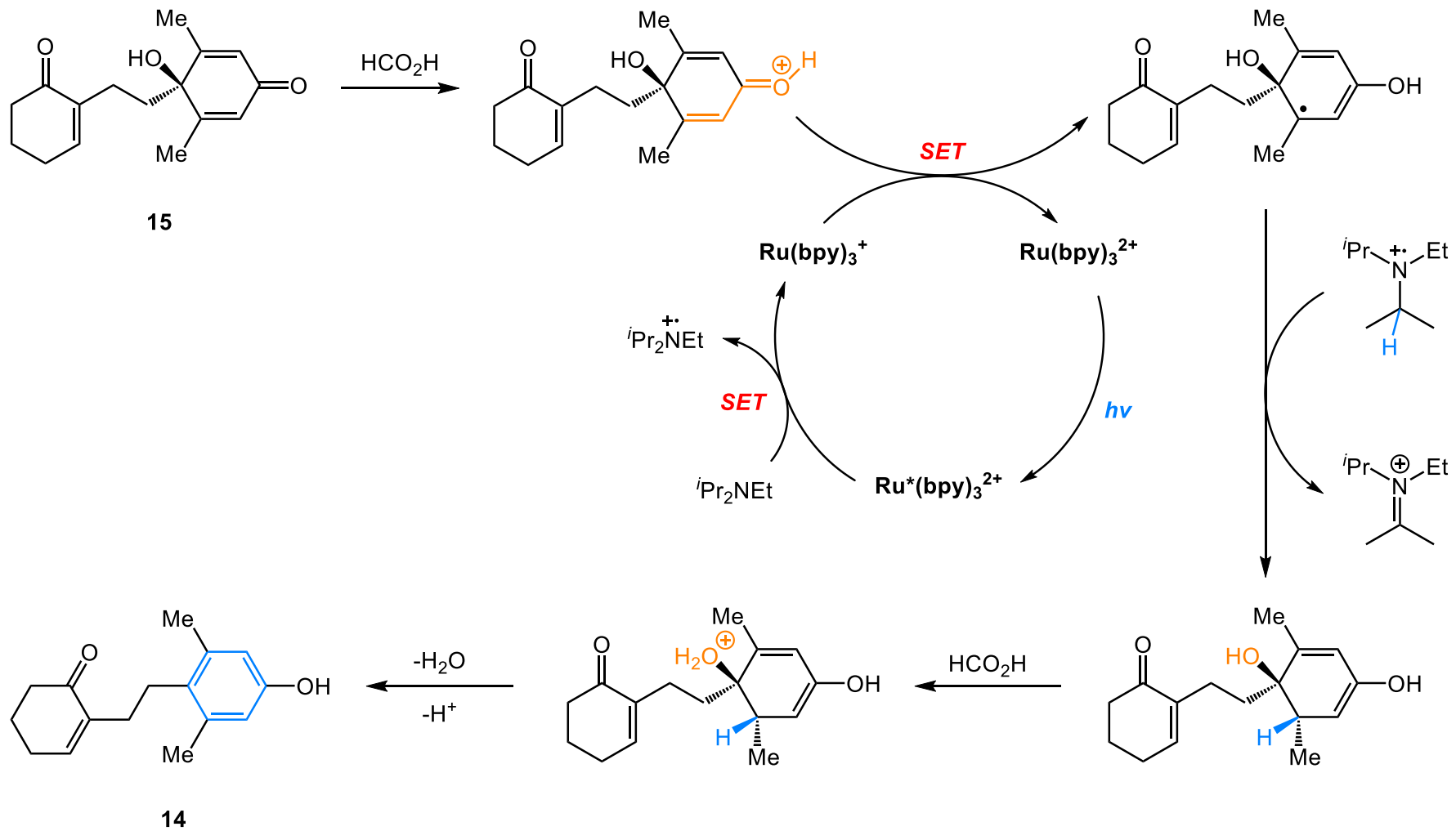
Retrosynthetic Analysis



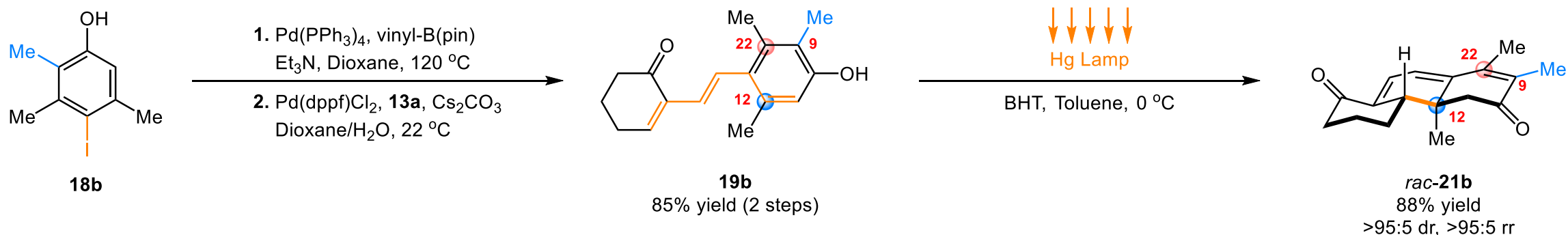
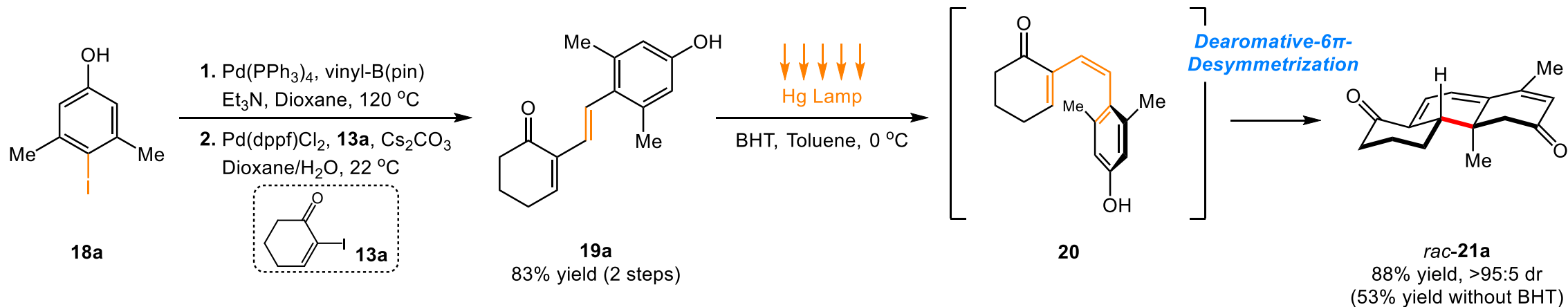
Synthetic Attempt



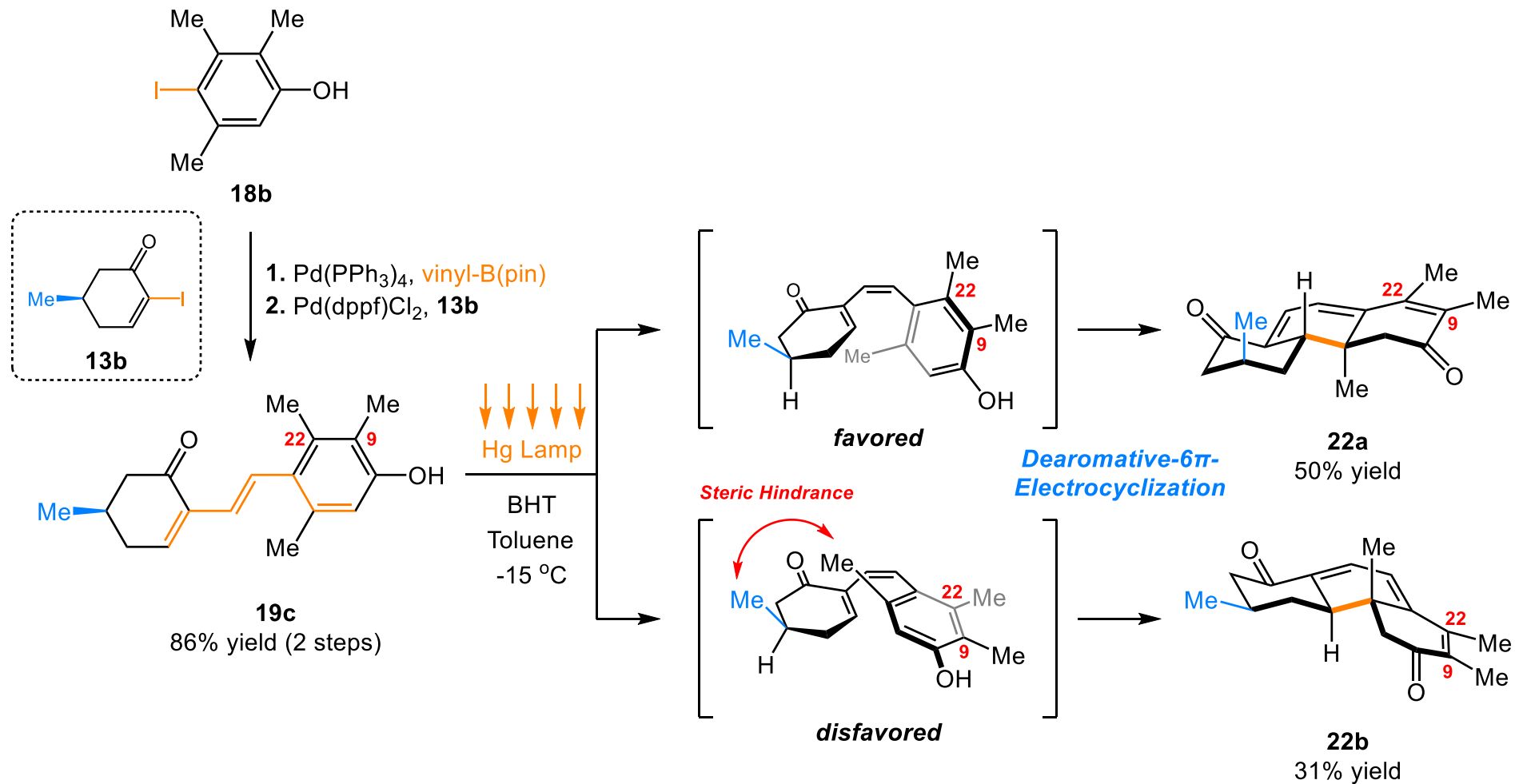
Mechanism of Compound 15 to 14



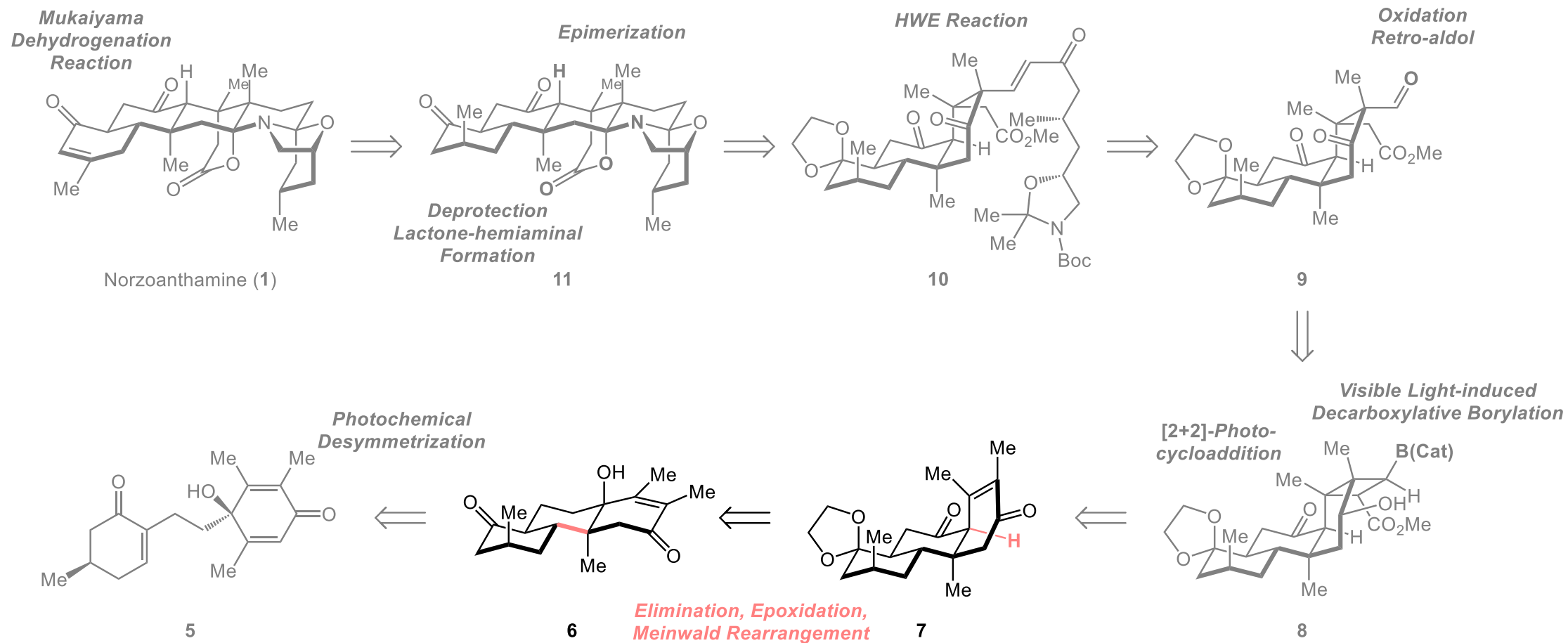
Synthetic Attempt



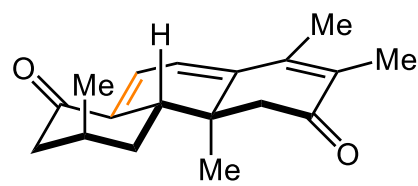
Synthesis of Compound 22



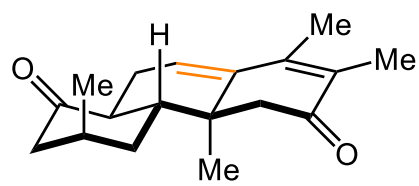
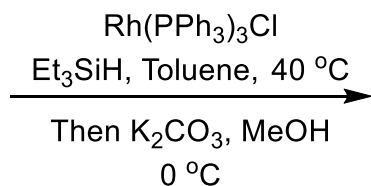
Retrosynthetic Analysis



Synthesis of Compound 7

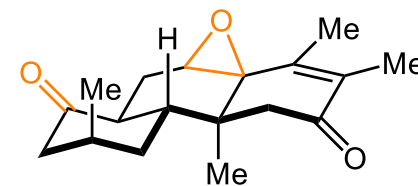
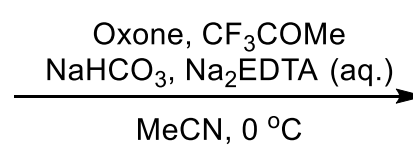


22a



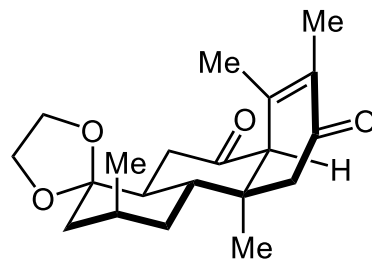
23

87% yield, >98:2 dr



24

96% yield, >98:2 dr



7

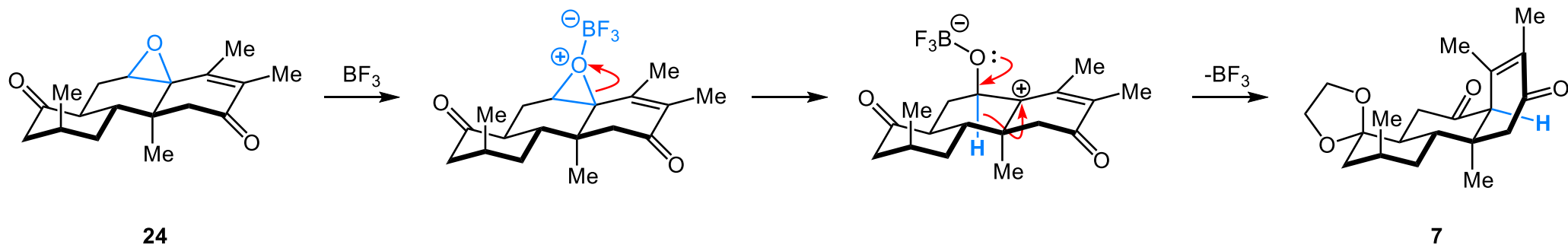
97% yield, >98:2 dr

Meinwald Rearrangement

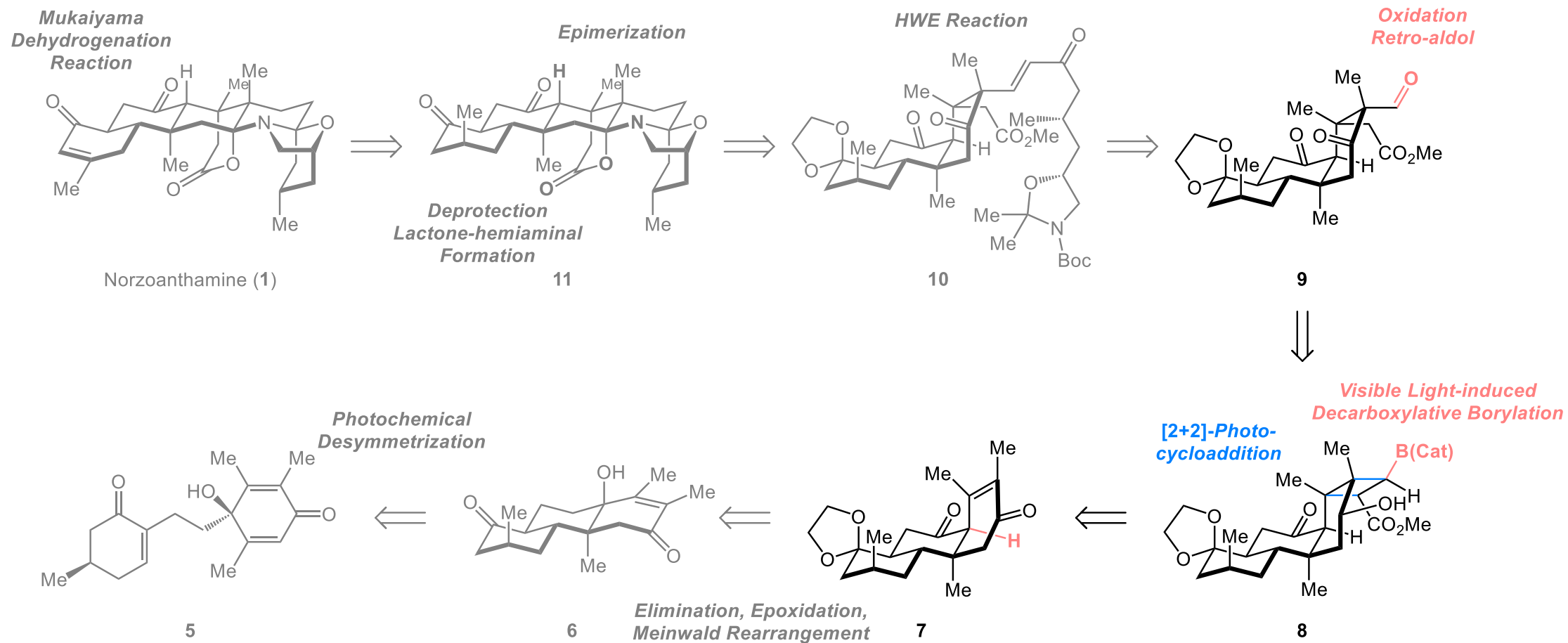
BF₃•Et₂O, DCM, 0 °C

Then 2-ethyl-2-methyl-1,3-dioxolane
22 °C

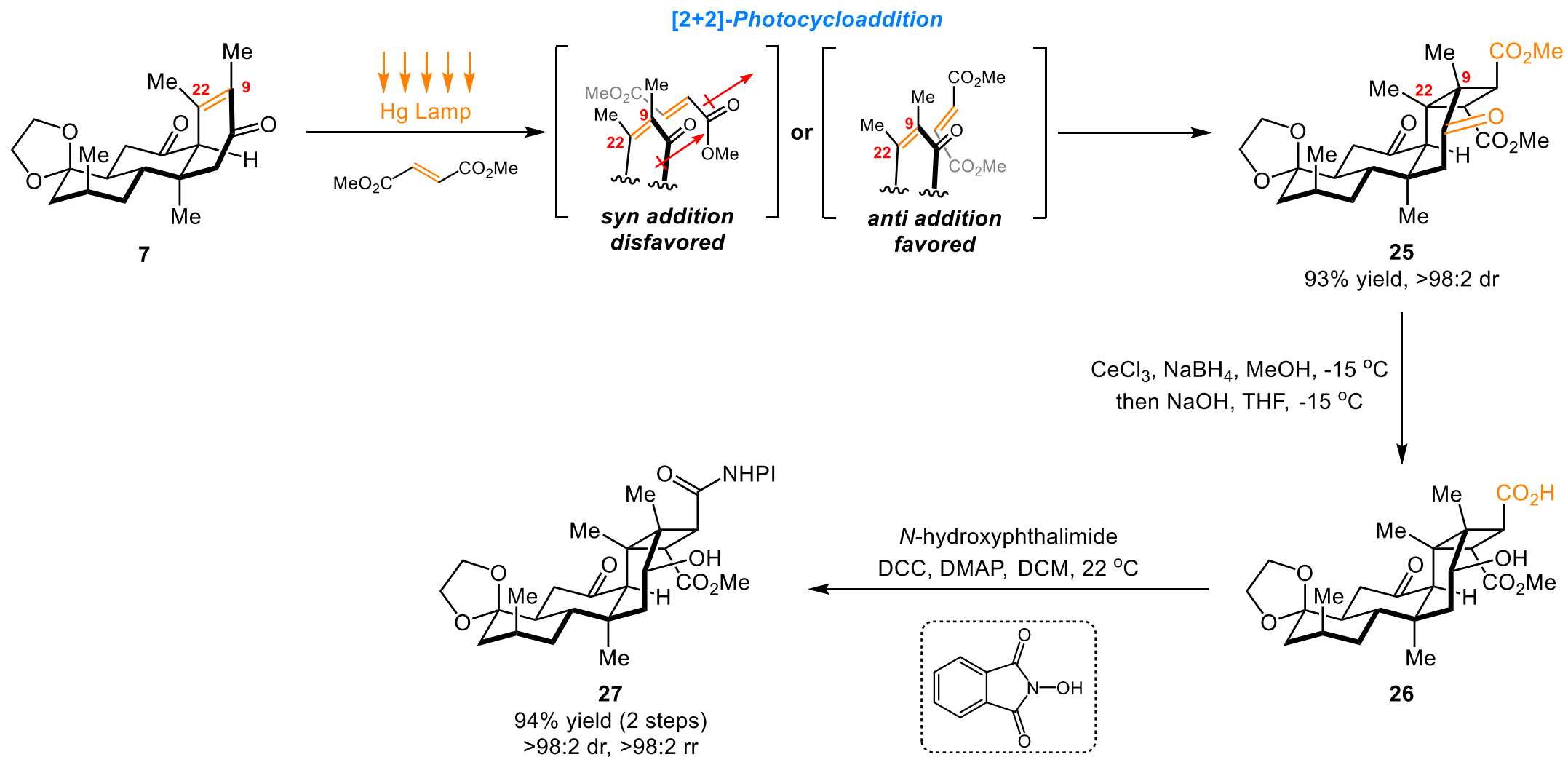
Meinwald Rearrangement



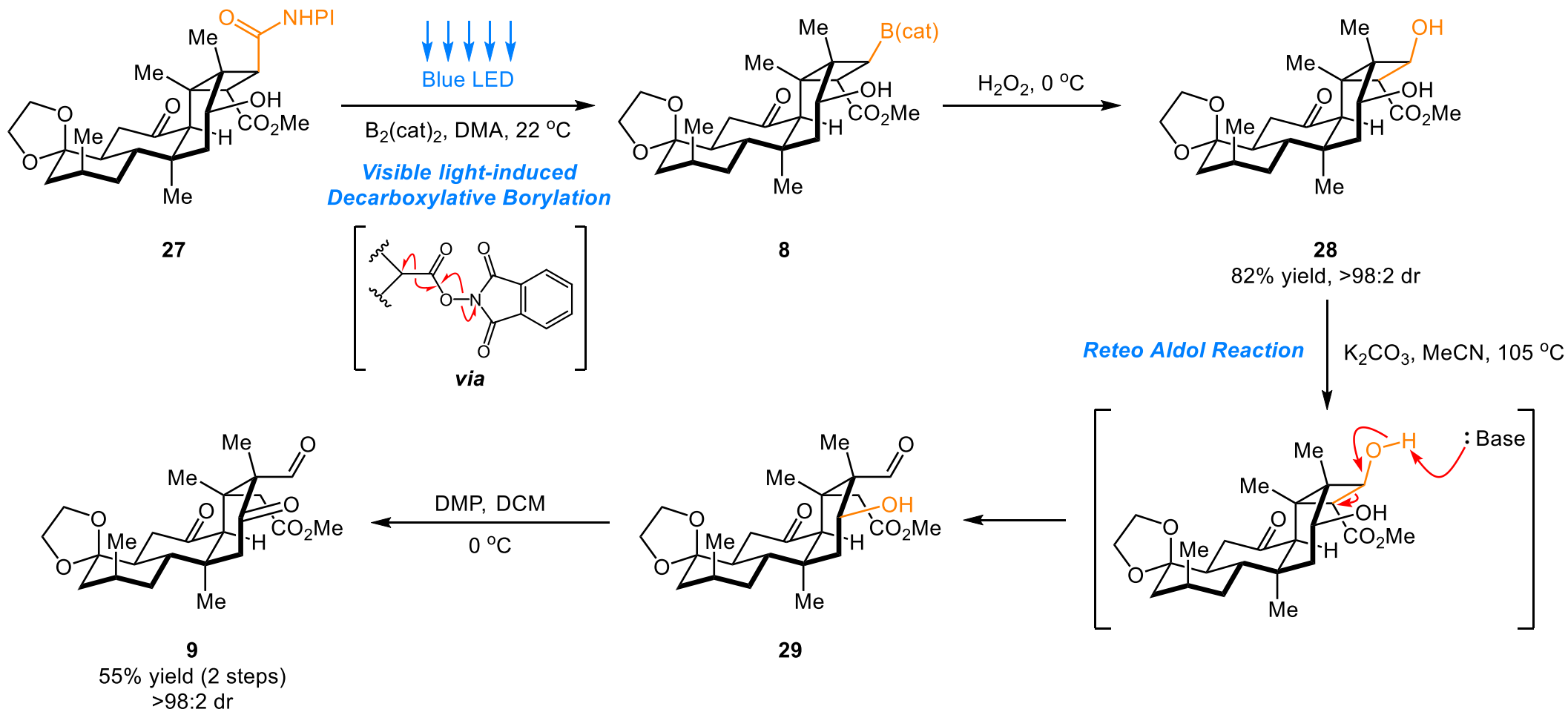
Retrosynthetic Analysis



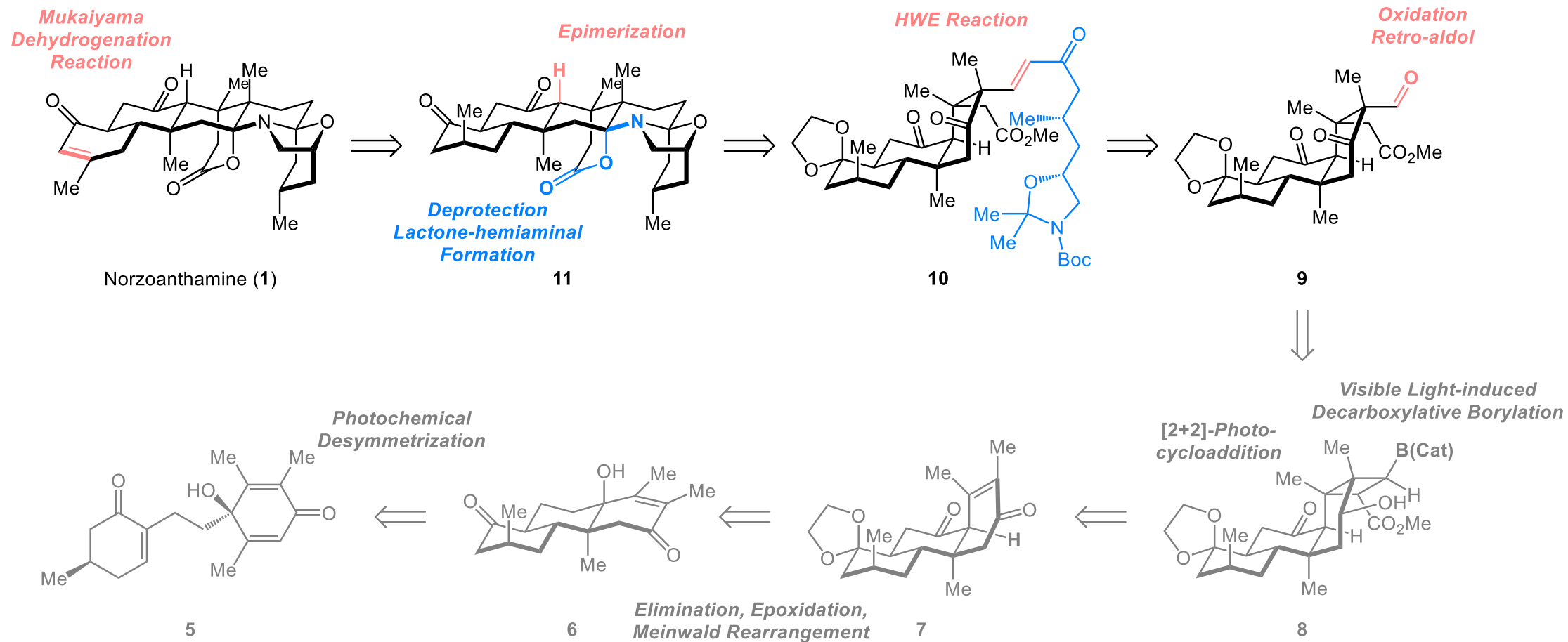
Synthesis of Compound 27



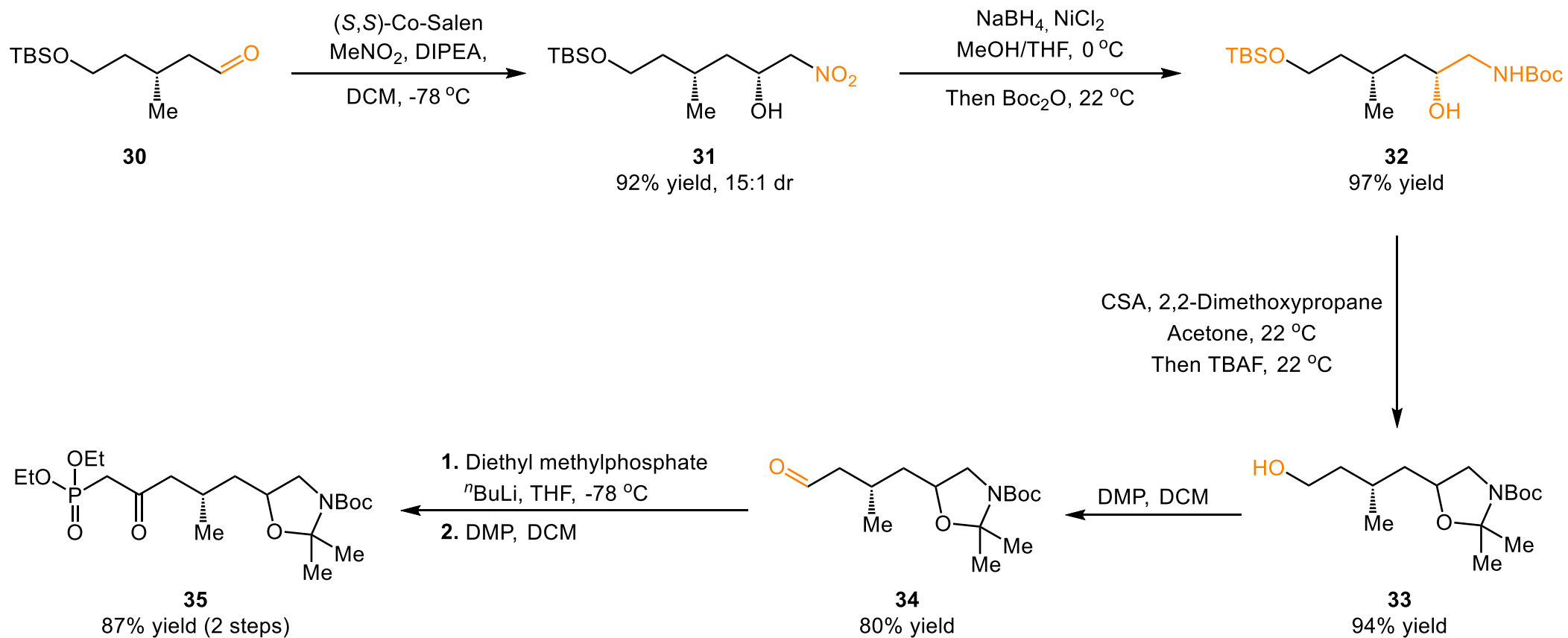
Synthesis of Compound 9



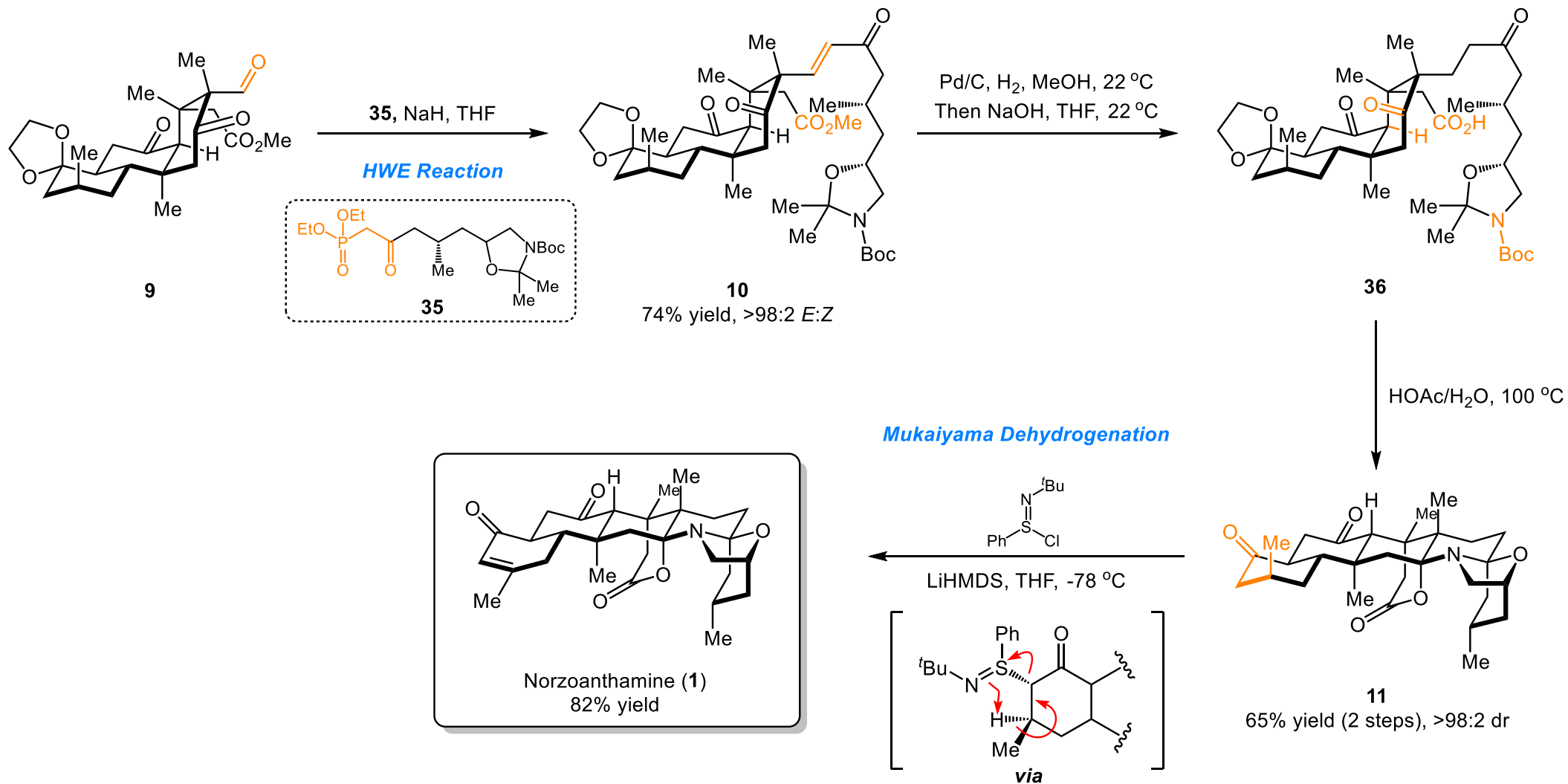
Retrosynthetic Analysis



Synthesis of Compound 35



Synthesis of Compound 1



Summary



- Dearomative-6 π -Electrocyclization
- [2+2]-Photocycloaddition
- Visible light-induced Decarboxylative Borylation

Sun, Y.; Zhang, X.; Jiang, F.; Zhang, M.; Wu, W.; Sun, Y. *J. Am. Chem. Soc.* **2024**, *146*, 32305

Writing Strategy

➤ First paragraph

Species and Structure



Biological Activities

- Zoanthamine alkaloids are architecturally distinct **polycyclic organic molecules isolated from colonial zoanths of the genus Zoanthus sp.**, a family of complex marine organisms. One member, norzoanthamine, has been found to mitigate osteoporosis symptoms in ovariectomized mice with fewer side effects than estrogen, which is considered a promising drug candidate for anti-osteoporotic or preventive therapy against bone deterioration.
- More recent investigations show that has **anti-angiogenic bioactivity and neuroprotective potential against paclitaxel-induced neurite damage**. Along with other congeners zoanthamine, oxyzoanthamine and 11-hydroxynorzoanthamine, zoanthamine alkaloids have also been found to express anti-tumor, anti-inflammation, anti-metastatic, and anti-platelet aggrega activity.

Writing Strategy

➤ Last paragraph

Summary



Challenges and
Committed Steps

- The strategies described here make it possible to synthesize the structurally complex marine alkaloid norzoanthamine efficiently. Sufficient amounts of the natural product can be accessed, enabling investigations regarding its potential for drug development. From a strategic point of view, the reliance of our approach on different photochemical processes underscores the importance of this class of transformations and their applicability in the efficient assembly of complex organic structures.
- While there is ample evidence for applying [2+2]-cycloadditions and their subsequent cleavage to natural product synthesis, others, such as decarboxylative borylation, to the best of our knowledge, have not been challenged in a similarly complicated setting. Congruent with this notion is that we needed to develop a photoinduced dearomative 6π desymmetrization method to be able to launch our investigations

Representative Examples

- **Rupturing** the cyclobutyl ring by means of a retro-aldol process was our next objective. (v. 使断裂; 使破裂)
- From a strategic point of view, the **reliance** of our approach on different photochemical processes underscores the importance of...(n. 依靠, 信任)
- **Congruent with** this notion is that we needed to develop a photoinduced dearomative 6π desymmetrization method to be able to launch our investigations. (与...相同/一致)

Acknowledgement

Thank You for Your Attention!