

# Literature Report II

## The total synthesis of (-)-Scabrolide A and enantioselective construction of Curcusones A–D

---

**Reporter: Li-Xia Liu**

**Checker: Xiang Li**

**Date: 2020-07-27**

Stoltz, B. M. *et al. J. Am. Chem. Soc.* **2020**, *142*, 8585.

Stoltz, B. M. *et al. Chem. Sci.* **2019**, *10*, 10562.

# Contents

---

- 1 Introduction**

---
- 2 Total synthesis of (-)-Scabrolide A**

---
- 3 Enantioselective construction of Curcusones A–D**

---
- 4 Summary**

---

# CV of Pr. Brian M. Stoltz

---



## Background:

- ❑ **1993** B.A. and B.S., Indiana University of Pennsylvania;
- ❑ **1996** M.A., Yale University;
- ❑ **1997** Ph.D. California Institute of Technology (Caltech);
- ❑ **2006** Assistant Professor, Caltech;
- ❑ **2007** Associate Professor, Caltech;
- ❑ **Now** Professor, Caltech.

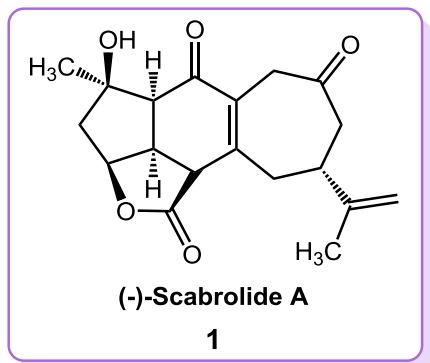
---

## Research:

Organic Synthetic Chemistry: the development and implementation of new strategies for the preparation of structurally complex molecules.

# Introduction

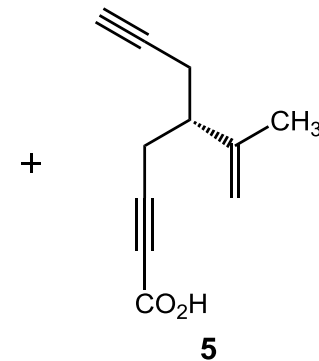
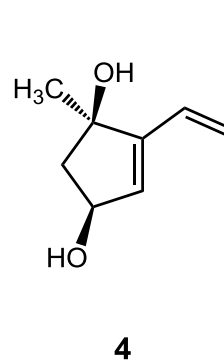
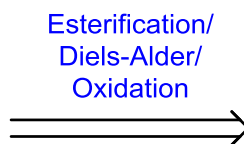
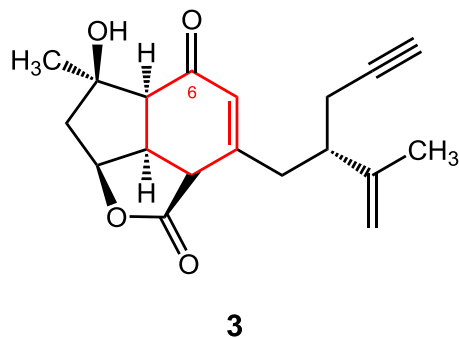
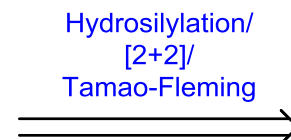
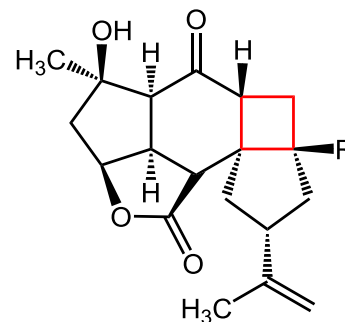
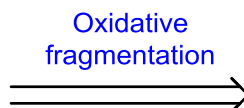
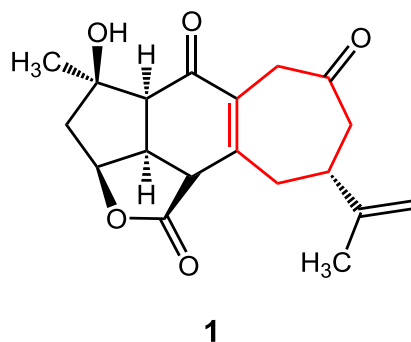
---



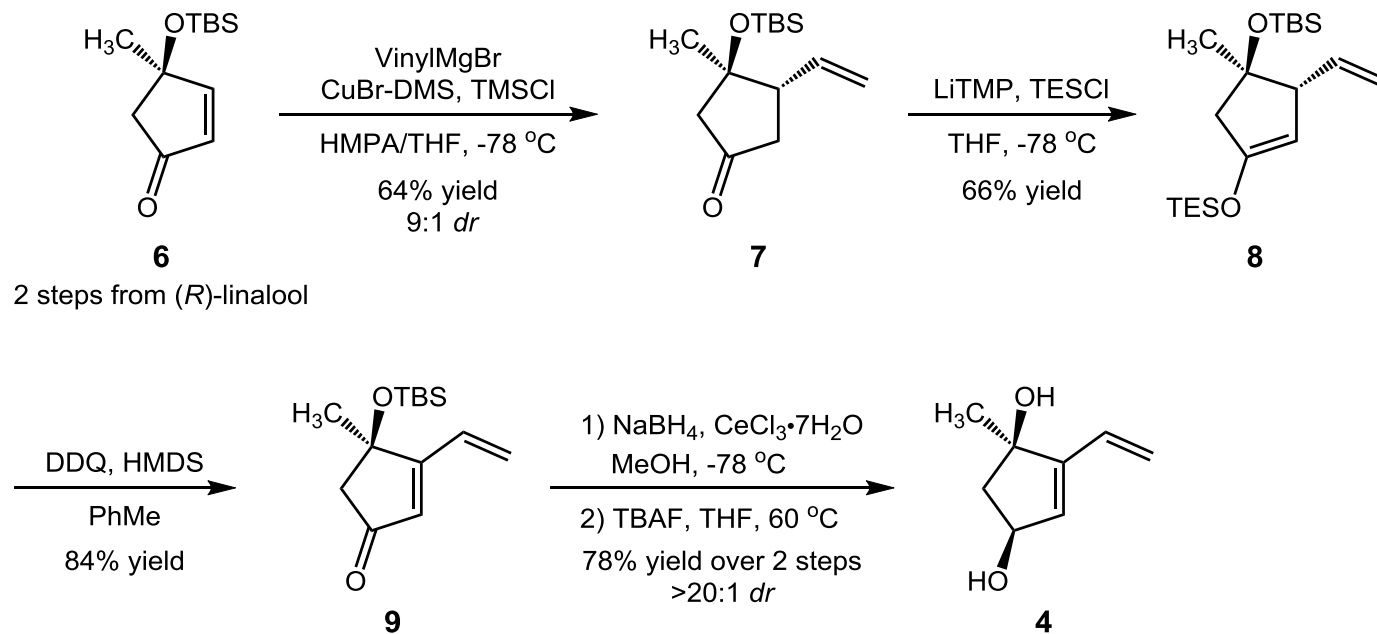
- Isolated from the *Sinularia* soft corals;
- Potential as an *anti*-inflammatory agent;
- [5–6–7] carbocyclic framework and six stereogenic centers.

Stoltz, B. M. *et al. J. Am. Chem. Soc.* **2020**, 142, 8585.

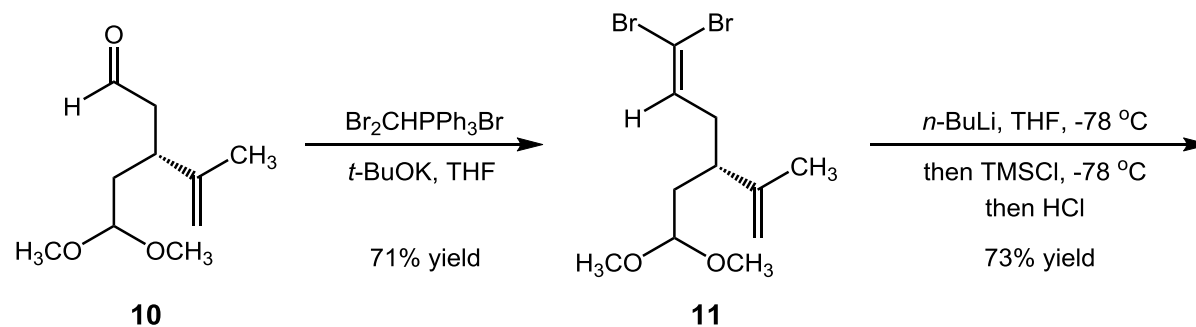
# Retrosynthetic Analysis of (-)-Scabrolide A



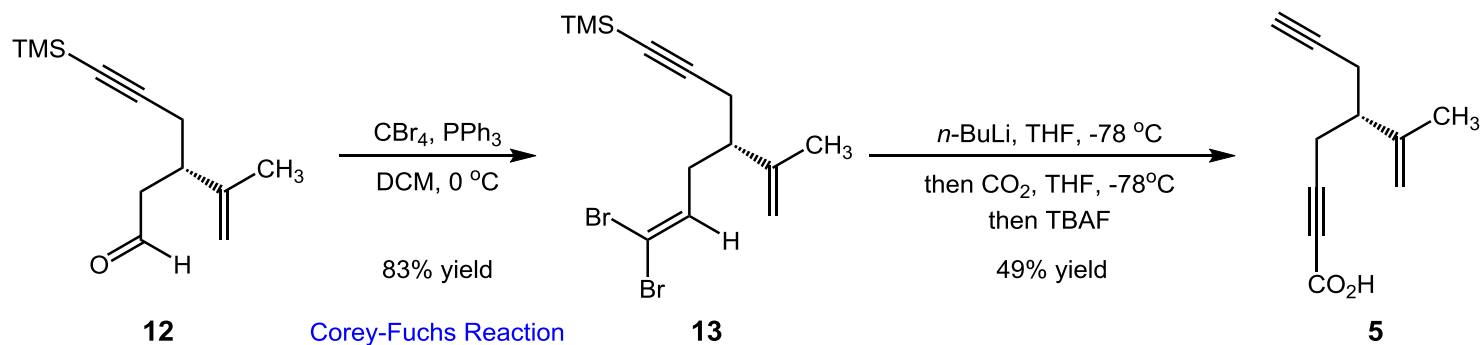
# Synthesis of Compound 4



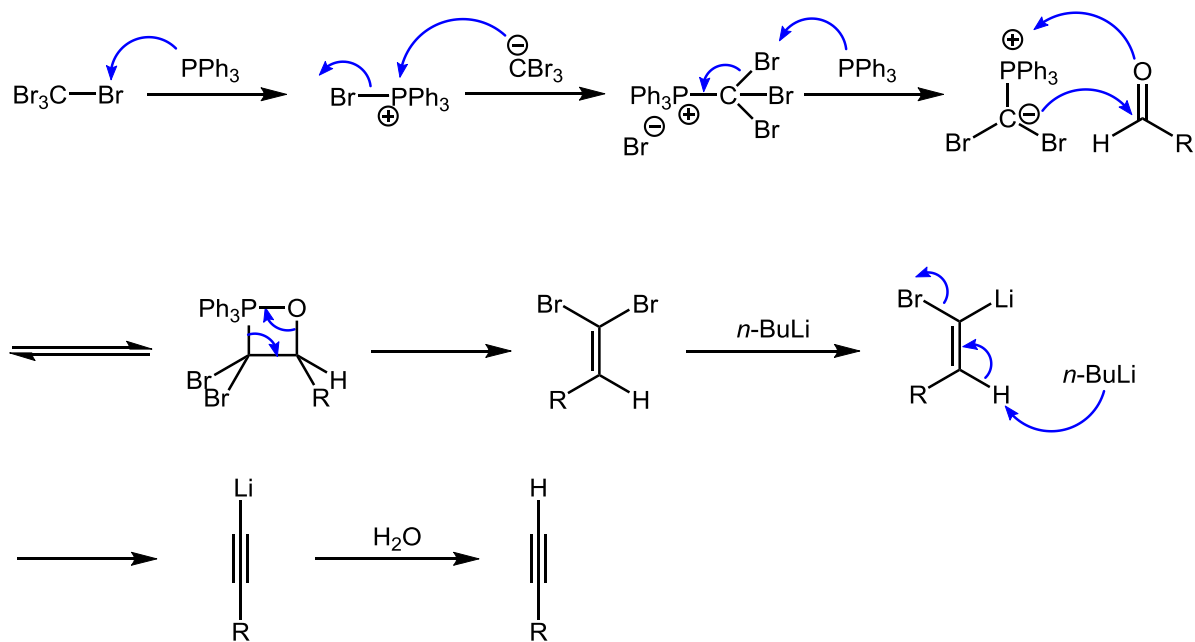
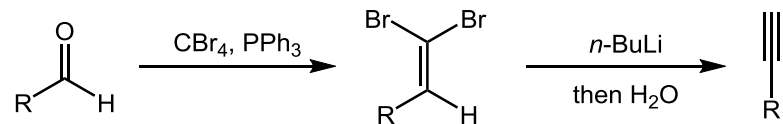
# Synthesis of Compound 5



5 steps from (*R*)-carvone



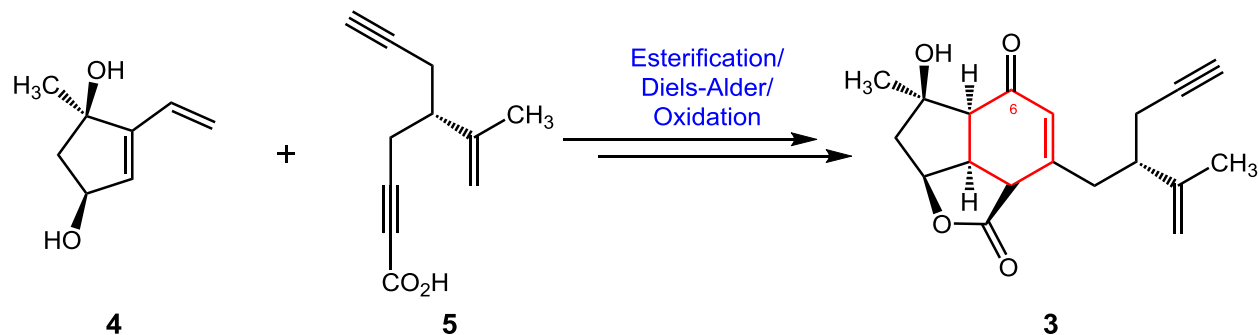
# Corey-Fuchs Reaction



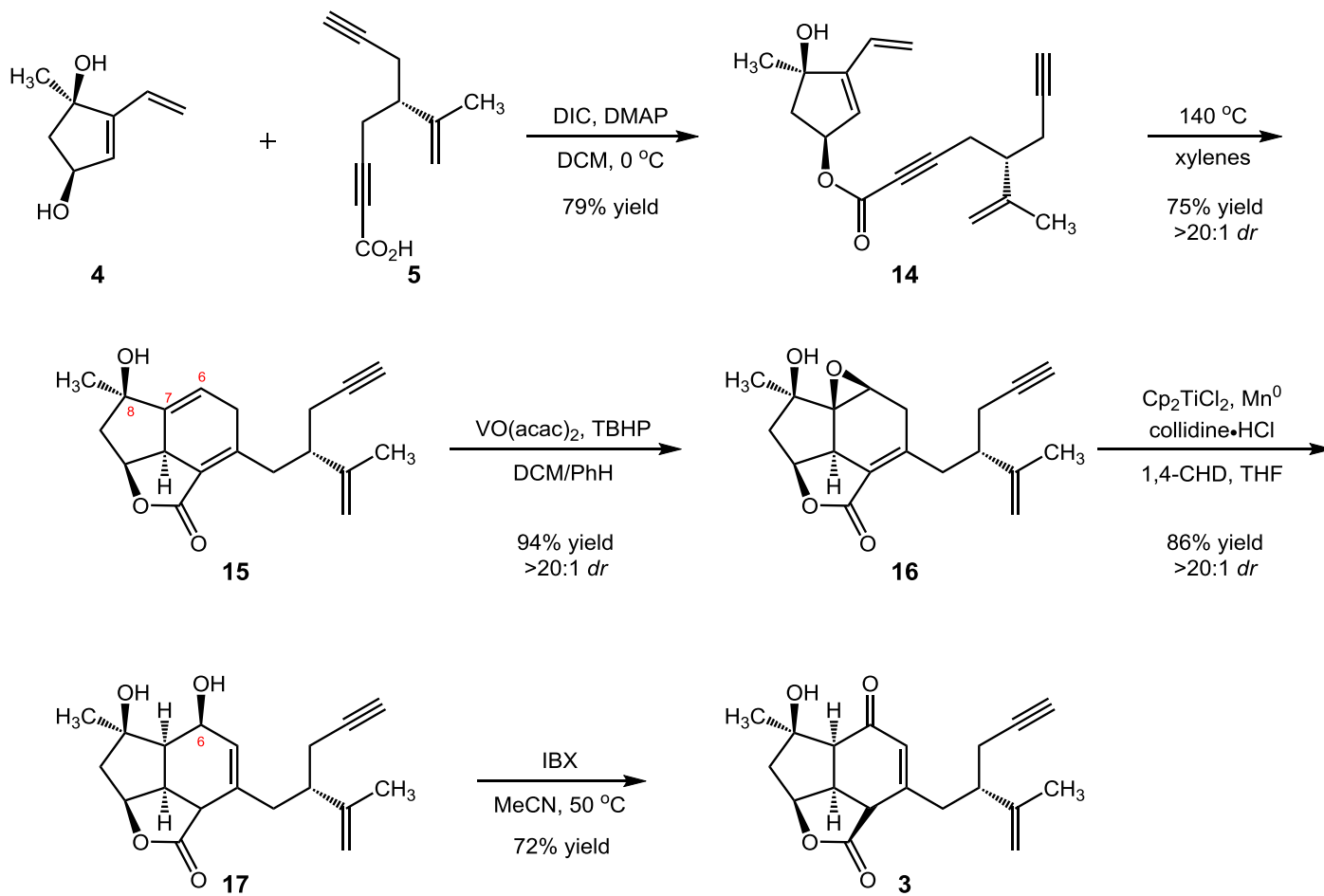


# Synthesis of Compound 3

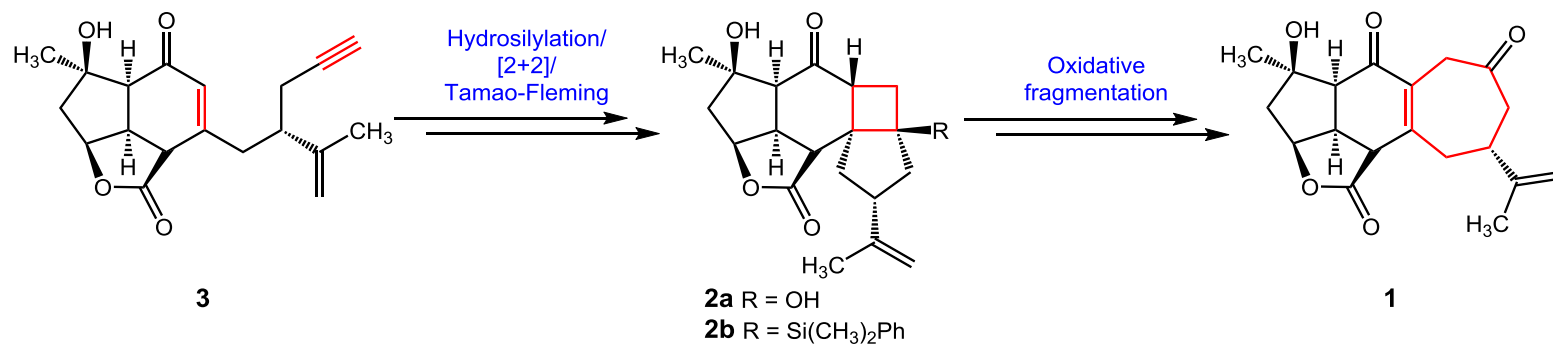
---



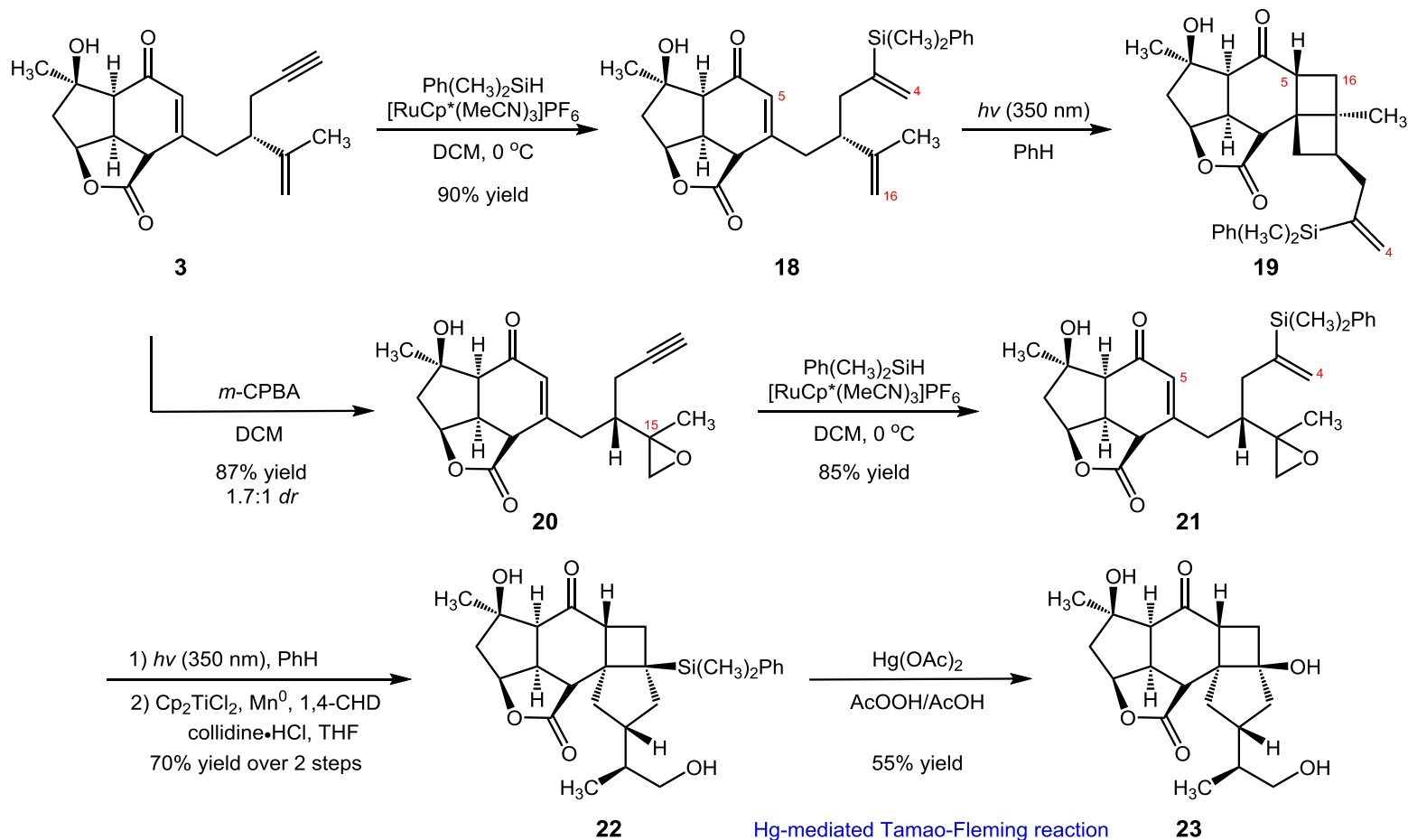
# Synthesis of Compound 3



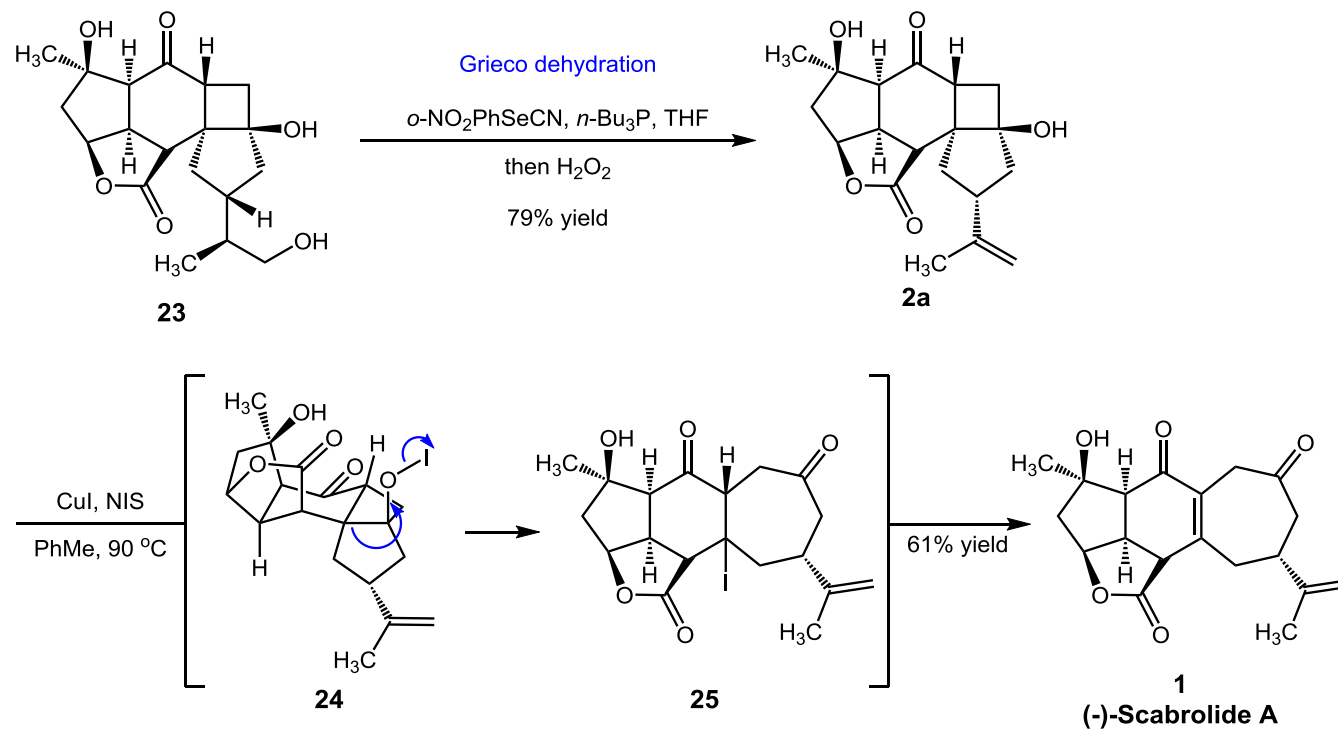
# Synthesis of Compound 1



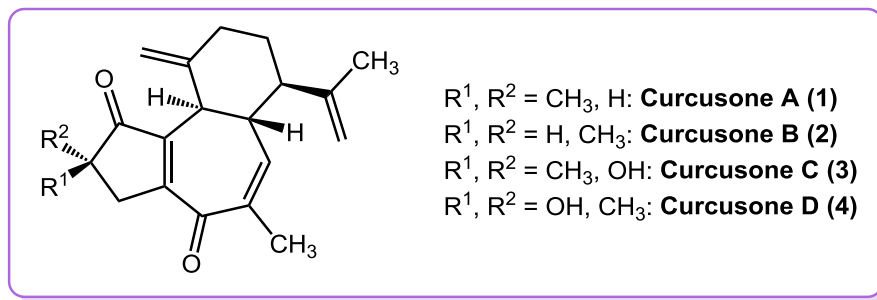
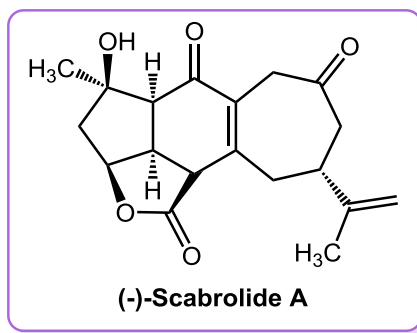
# Synthesis of Compound 23



# Synthesis of (-)-Scabrolide A

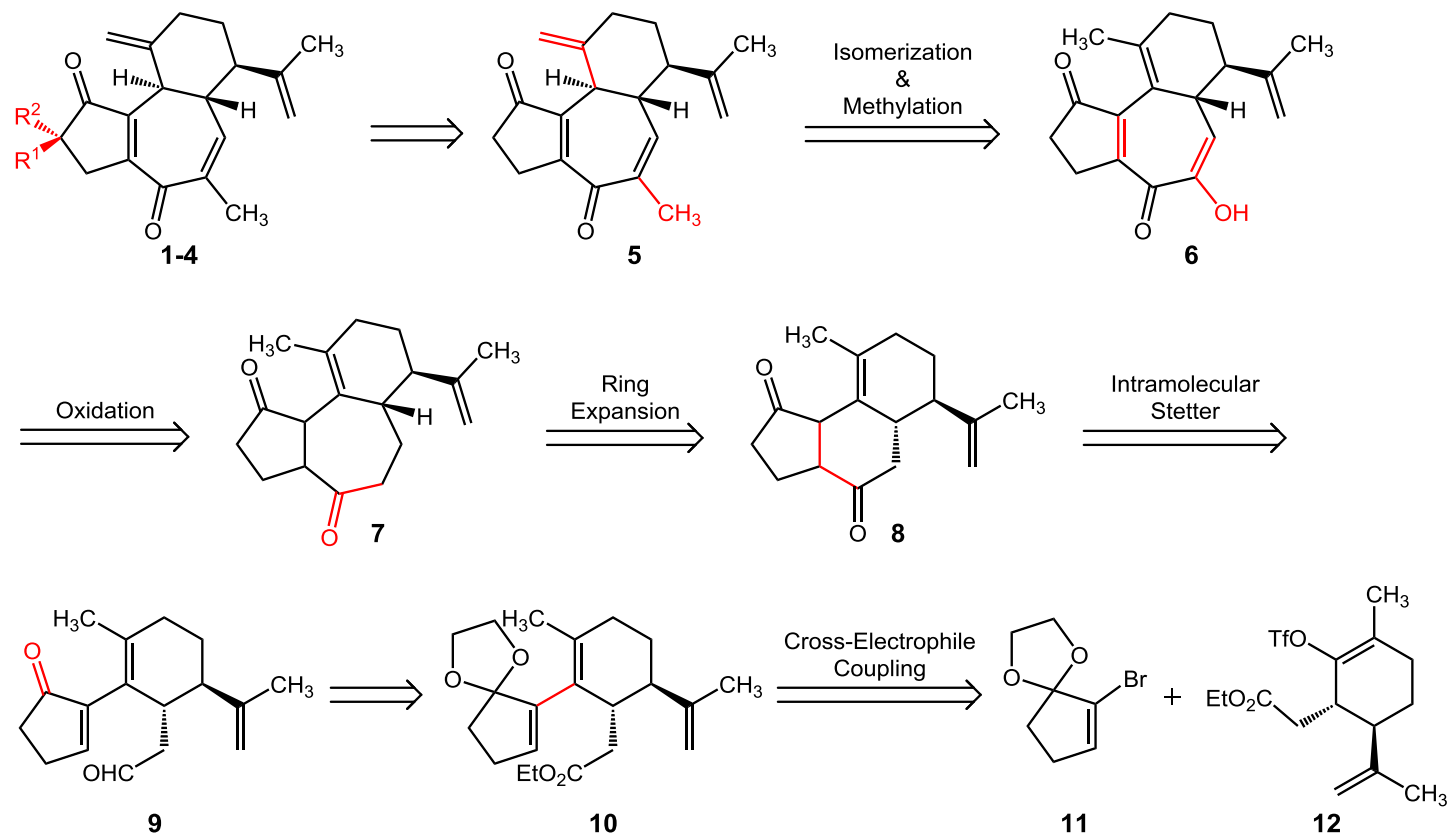


# Introduction

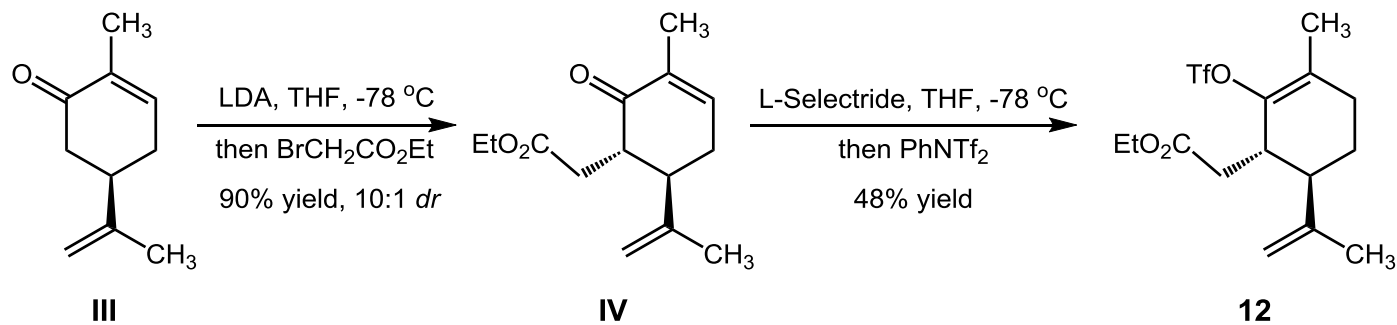
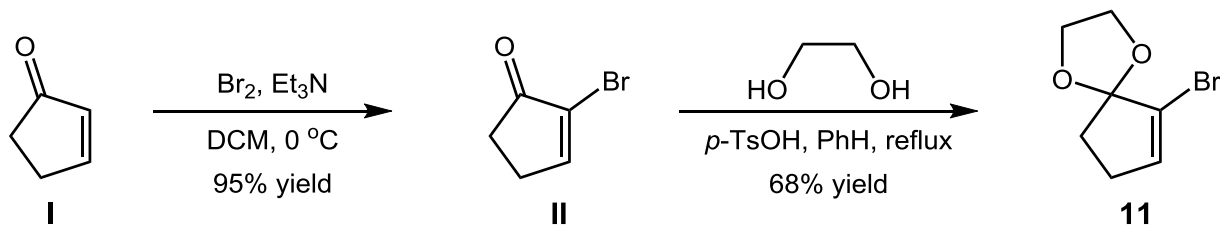


Stoltz, B. M. *et al. Chem. Sci.* **2019**, *10*, 10562.

# Retrosynthetic Analysis of Curcusones A–D

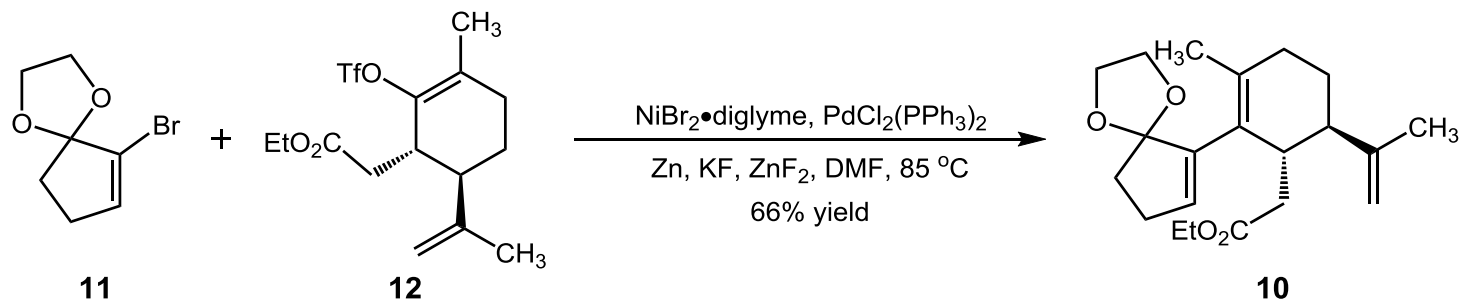


# Synthesis of Compound 11 and 12

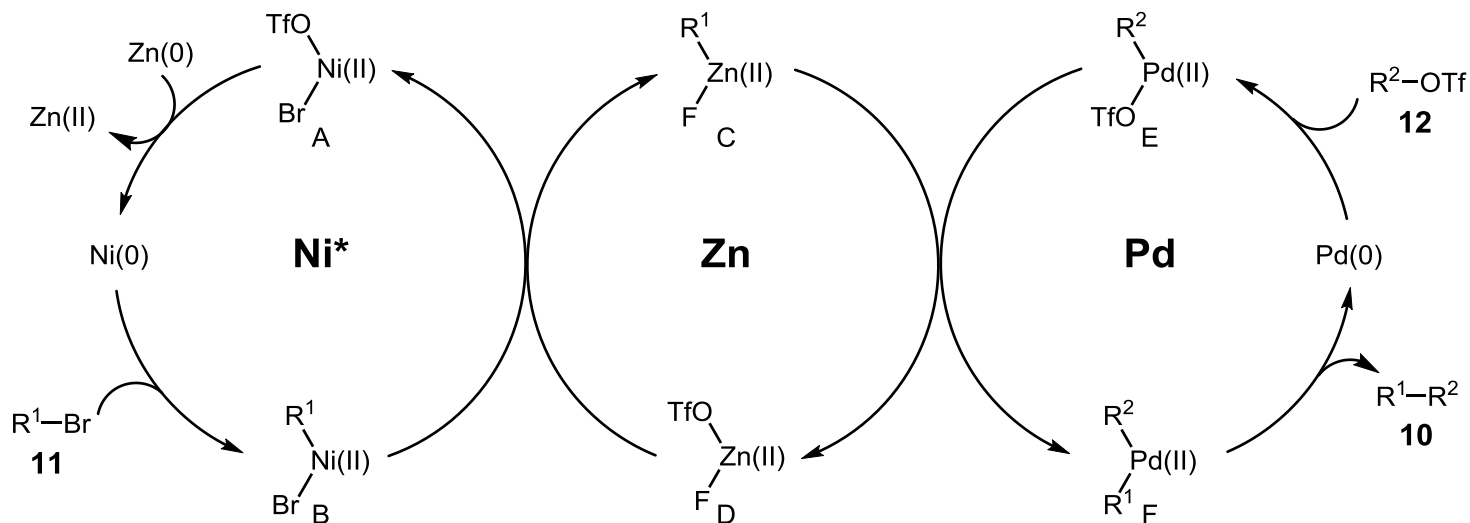




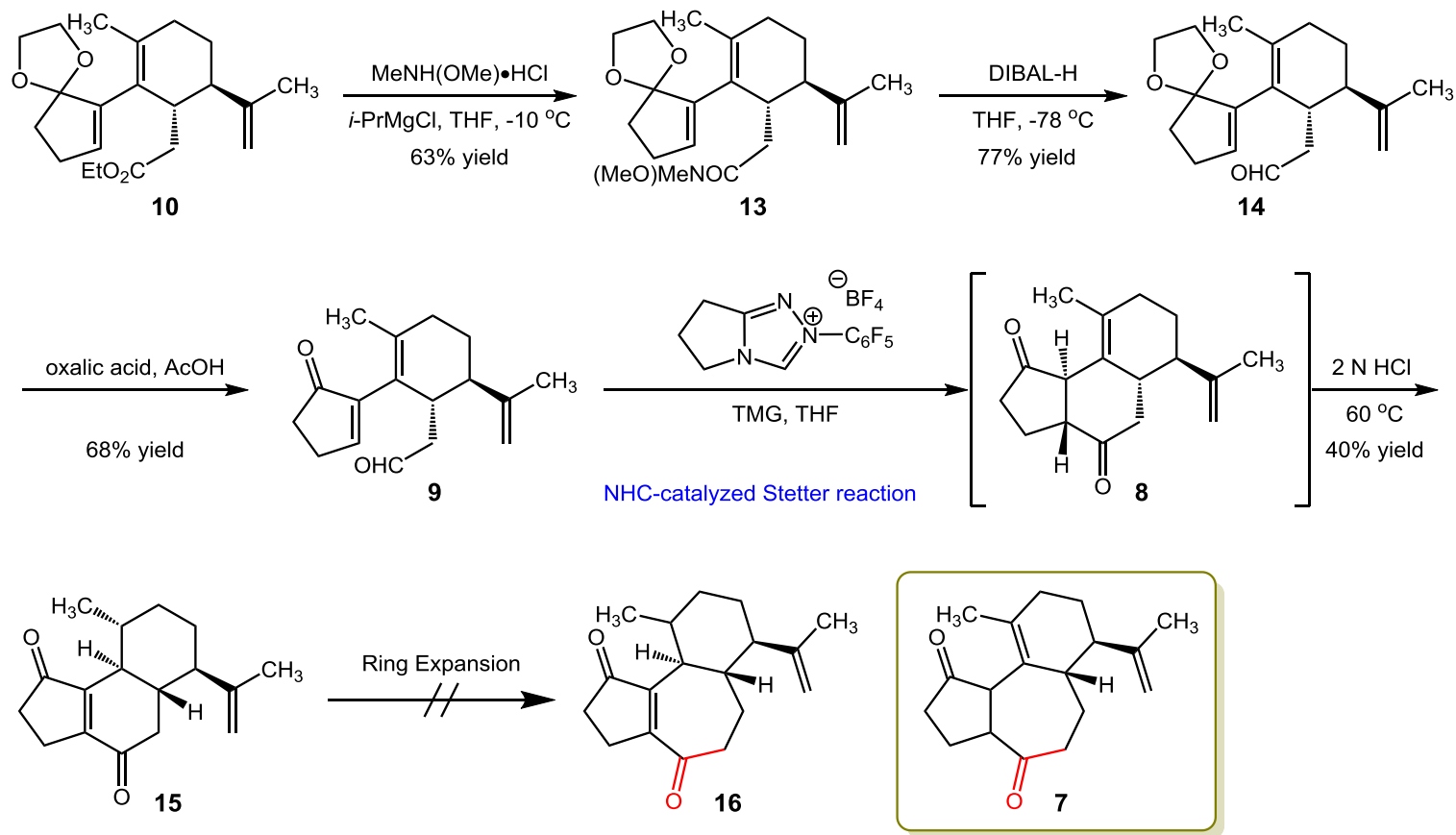
# Synthesis of Compound 10



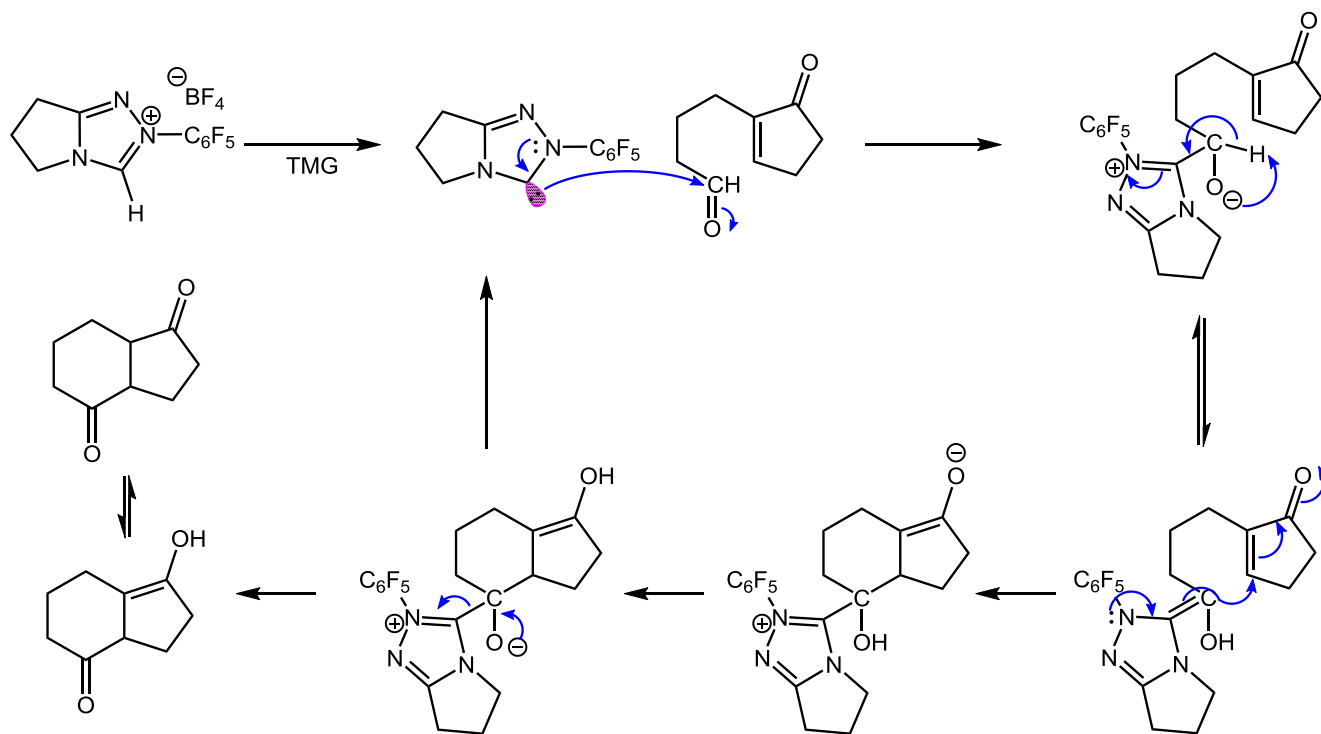
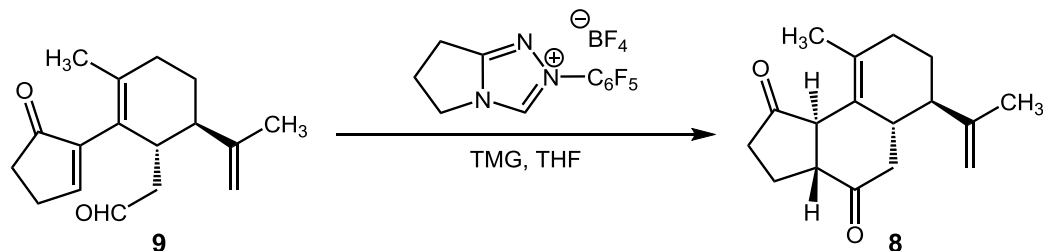
Proposed mechanism



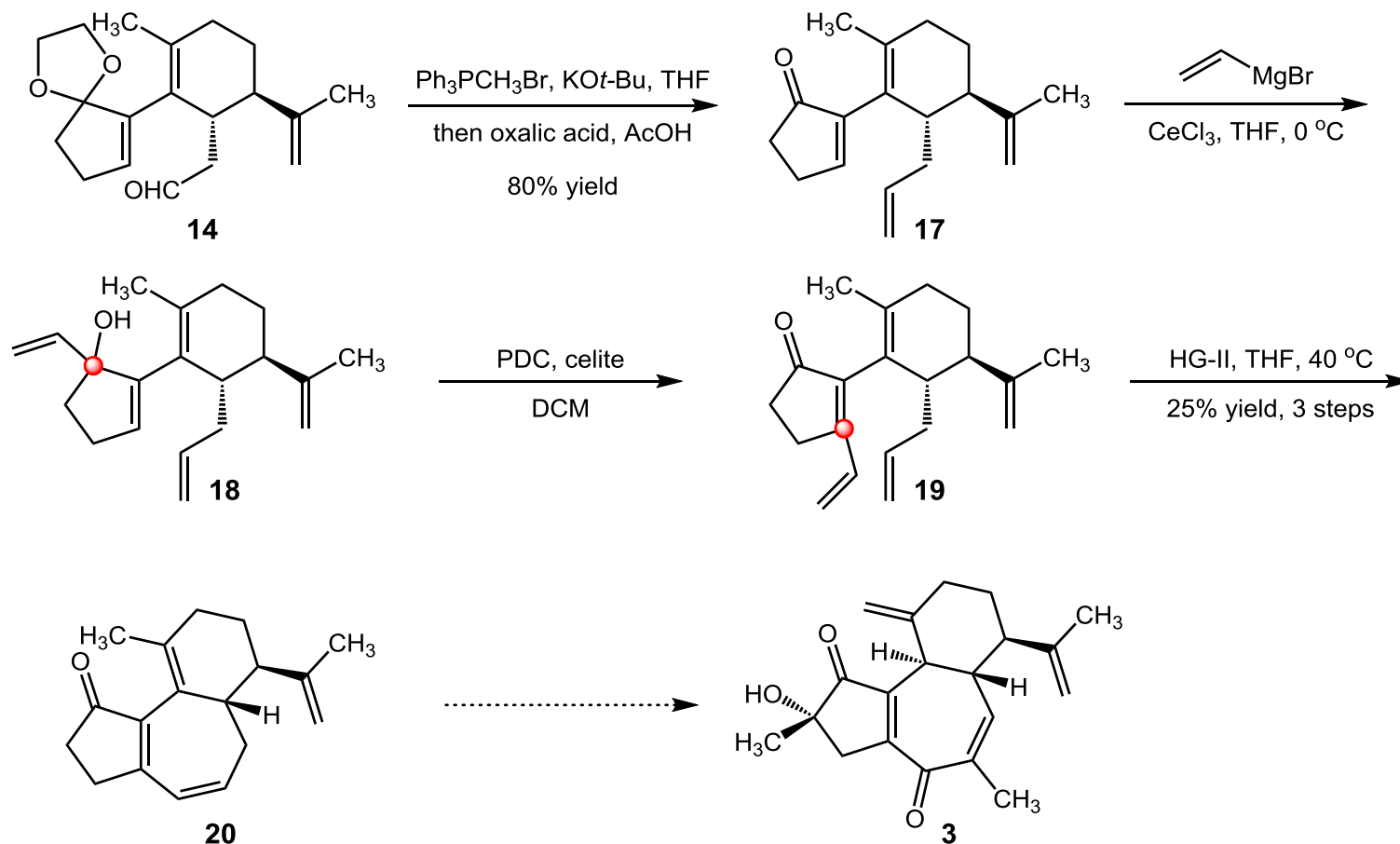
# Synthesis of Compound 15



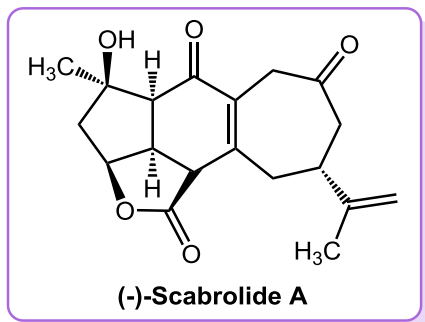
# Proposed Mechanism



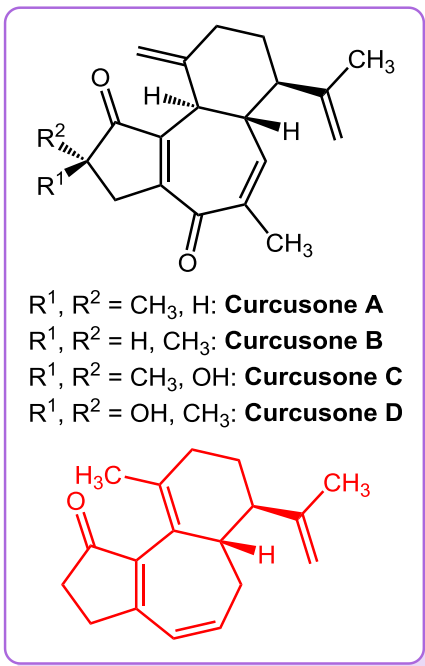
# Synthesis of the tricyclic core of Curcusones



# Summary



- 17 Total steps, 1.3% overall yield
- Intramolecular Diels–Alder reaction
- Intramolecular [2+2] cycloaddition/fragmentation



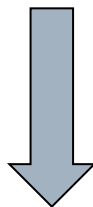
- 9 Total steps, 4.1% overall yield
- Ring-Closing Metathesis (RCM)
- Cross-electrophile coupling strategy

Stoltz, B. M. *et al. J. Am. Chem. Soc.* **2020**, 142, 8585.  
Stoltz, B. M. *et al. Chem. Sci.* **2019**, 10, 10562.

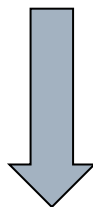
# The First Paragraph

---

天然产物的来源



结构特点



合成困难

# The First Paragraph

---

The polycyclic furanobutenolide-derived norcembranoid diterpenoids comprise a family of complex and structurally diverse C<sub>19</sub> marine natural products isolated from the *Sinularia* soft corals. Biosynthetically, these isomeric compounds are believed to arise from the macrocyclic furanobutenolide norcembranoids following a divergent series of intramolecular cyclizations, which give rise to the diverse set of fused ring systems characterizing this natural product class. Specifically, members of this family typically feature complex, polycyclic carbon frameworks decorated with abundant and synthetically challenging oxygenation patterns and stereochemical arrays.

# The First Paragraph

---

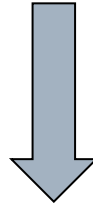
Consequently, despite intense interest from the synthetic community over the past two decades, the polycyclic furanobutenolide-derived norcembranoids have thus far evaded all total synthesis efforts, highlighting their difficulty as synthetic targets.



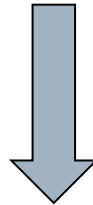
# The Last Paragraph

---

工作的重要性



合成的特点



工作的意义

# The Last Paragraph

---

In conclusion, we have disclosed the first total synthesis of the norcembranoid diterpenoid (-)-scabrolide A. To our knowledge, this report constitutes the first total synthesis of any member of the polycyclic furanobutenolide-derived norcembranoid diterpenoid family, a class of natural products that have evaded synthetic efforts for the more than two decades since their initial isolation. The route exploits the convergent esterification and subsequent intramolecular Diels–Alder cycloaddition of two enantiopure fragments to introduce each of the 19 carbon atoms of the natural product. An initially unsuccessful [2+2] cycloaddition was enabled by an unconventional olefin protection strategy, which allows for the correct regiochemical outcome of this key reaction.

# The Last Paragraph

---

Finally, a late-stage oxidative cyclobutanol fragmentation was employed to furnish the cycloheptenone ring and complete the total synthesis. Efforts are currently ongoing to extend this synthetic strategy toward the synthesis of other polycyclic furanobutenolide-derived norcembranoids, and progress will be reported in due course.

# Representative Examples

---

Biosynthetically, these isomeric compounds are believed to arise from the macrocyclic furanobutenolide norcembranoids following a divergent series of intramolecular cyclizations, which give rise to the diverse set of fused ring systems characterizing this natural product class.(...一系列不同的...产生各种各样的)

Faced with this issue of regioselectivity in the photocycloaddition, we opted to re-engineer our route accordingly.(面对...问题，我们选择了...)

The structure of triols 25 and C(15)-epi-25 (not shown, see SI) were each unambiguously determined via X-ray diffraction, verifying the relative stereochemical configuration about the cyclobutane ring established in the [2+2] cycloaddition.(...均通过X射线衍射明确确定，验证了...的相对立体化学构型)

# Acknowledgement

---

***Thanks  
for your attention***