Literature Report II

Taming Shapeshifting Anions: Total Synthesis of Ocellatusone C

Reporter: Zheng Liu

Checker: Yu-Qing Bai

Sanchez, A.; Maimone, T. J.* *J. Am. Chem. Soc.* **2022**, *144*, 7594

2022-07-18

CV of A/Prof. Thomas J. Maimone

Background:

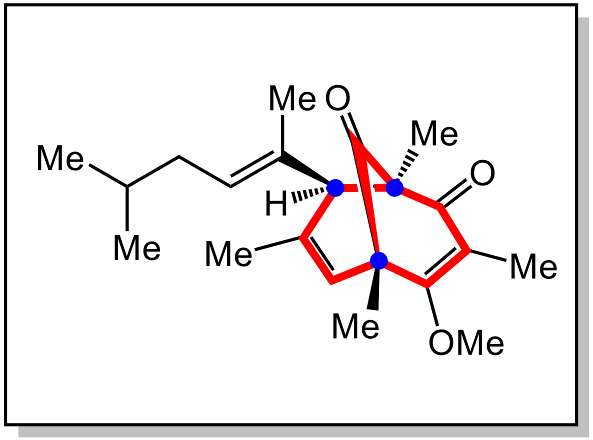
- ☐ **2000-2004** B.S., University of California, Berkeley
- ☐ **2004-2009** Ph.D., The Scripps Research Institute
- ☐ **2009-2012** NIH Postdoctoral Fellow, MIT
- ☐ **2012-2018** Assistant Professor, UC Berkeley
- ☐ **2018-now** Associate Professor, UC Berkeley

Research:

1. Total synthesis;
2. New methods for organic synthesis;
3. The synthesis of new catalyst architectures.

Contents

Introduction



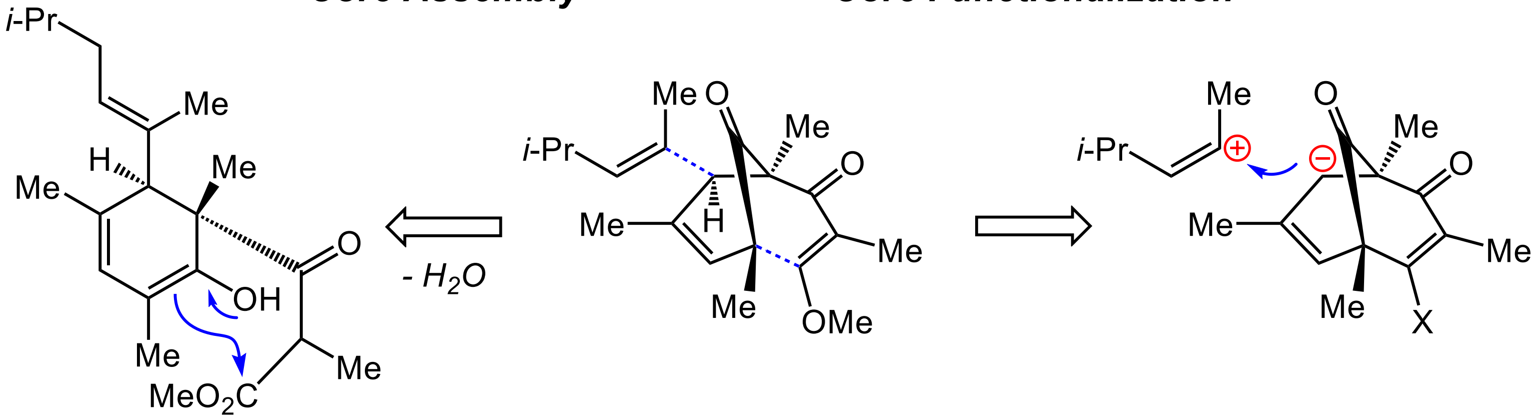
Ocellatusone C

Placobranchus ocellatus

- Isolated from *Placobranchus ocellatus* and characterized in 2020;
- Contain [3.3.1]-bicyclic core with three chiral centers.

Wu, Q.; Li, S.-W.; Xu, H.; Li, X.-W.* *et al. Angew. Chem. Int. Ed.* **2020**, *59,* 12105

Retrosynthetic Analysis



Late-stage Core Assembly

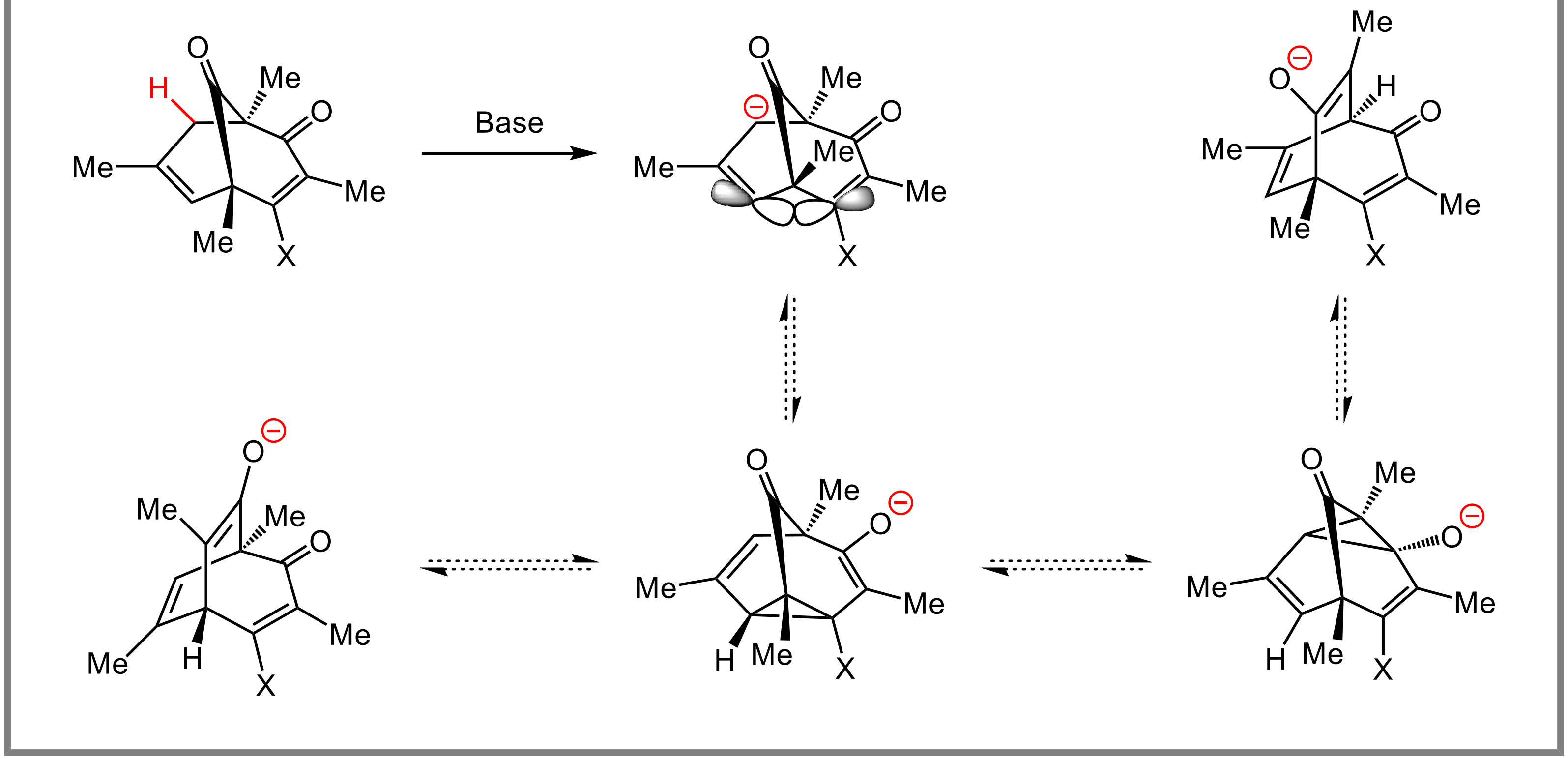
Late-stage Core Functionalization

Biosynthesis

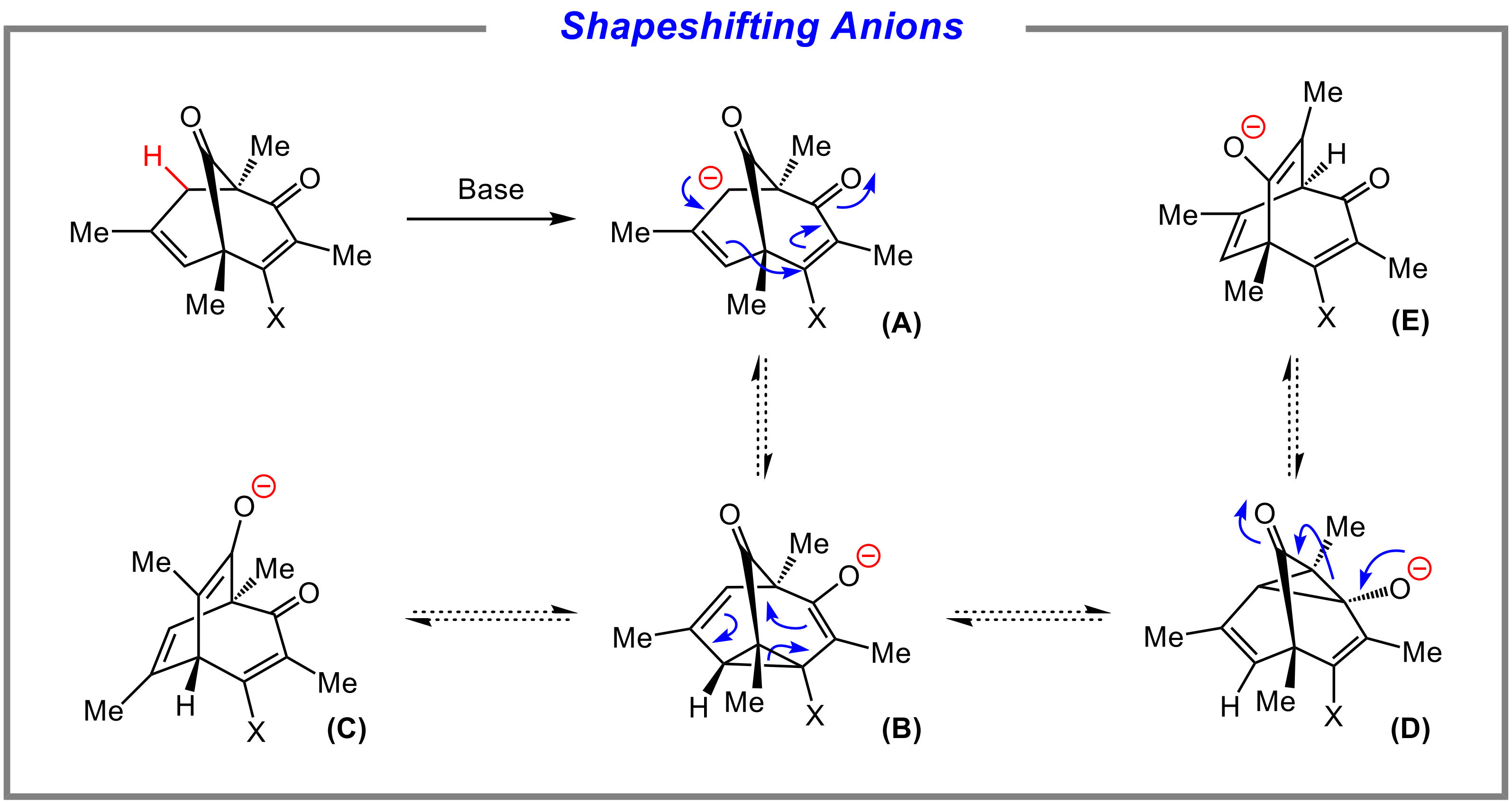
Retrosynthesis

Retrosynthetic Analysis

Shapeshifting Anions



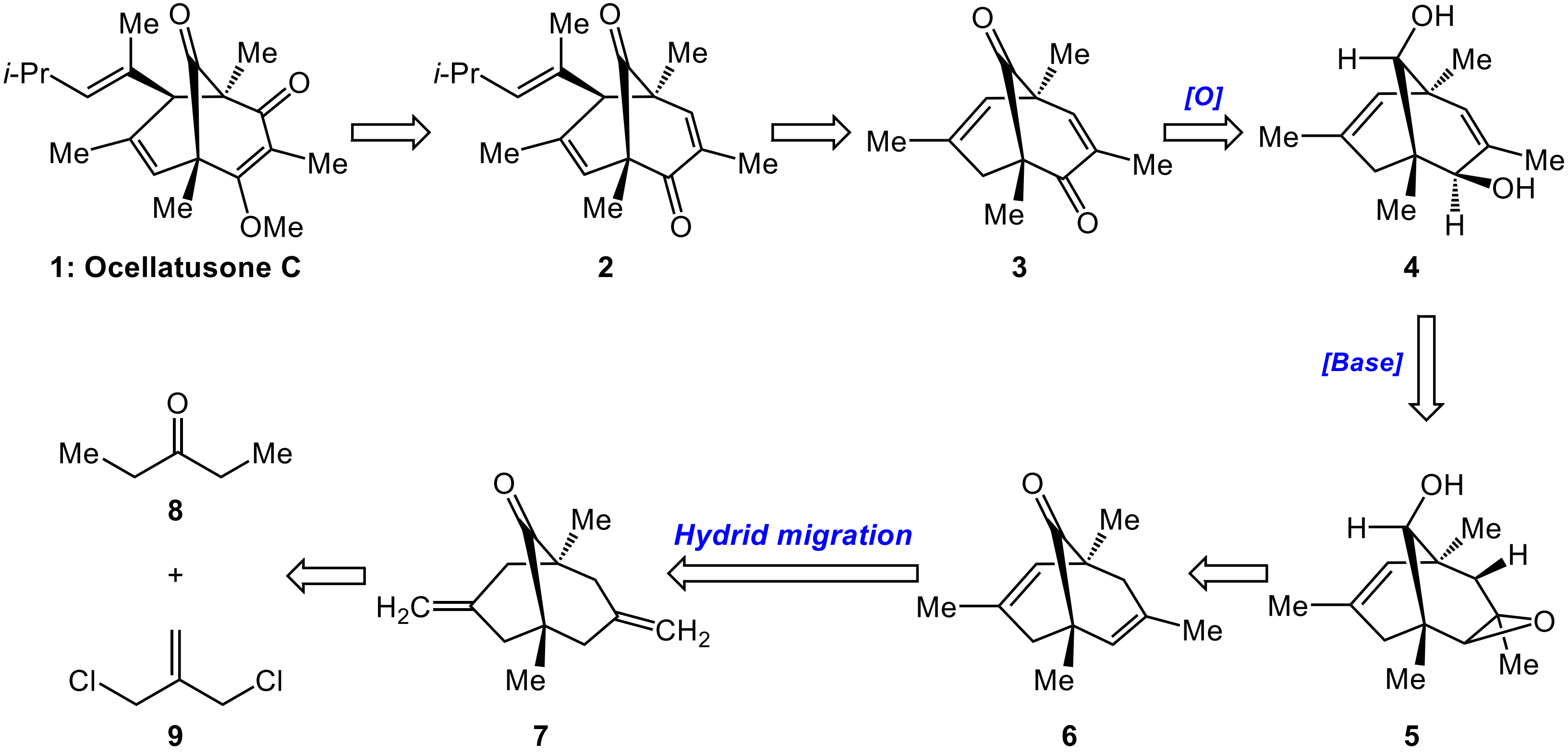
Retrosynthetic Analysis



◆ 多互变异构体

◆ 多反应位点

Retrosynthetic Analysis



1: Ocellatusone C

2

3

4

5

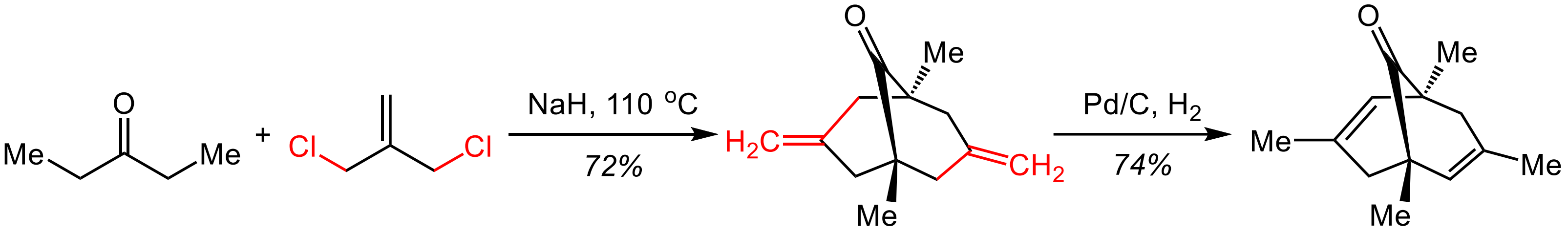
6

7

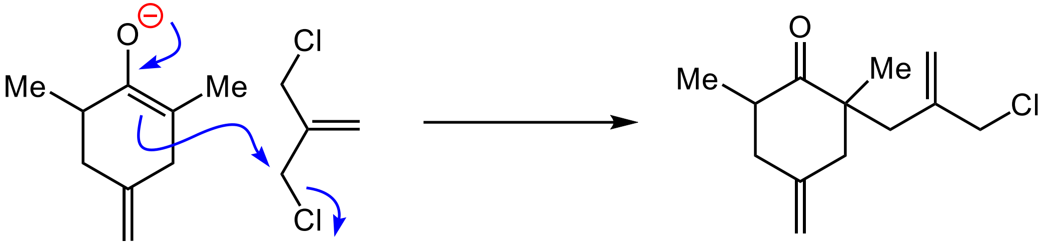
8

9

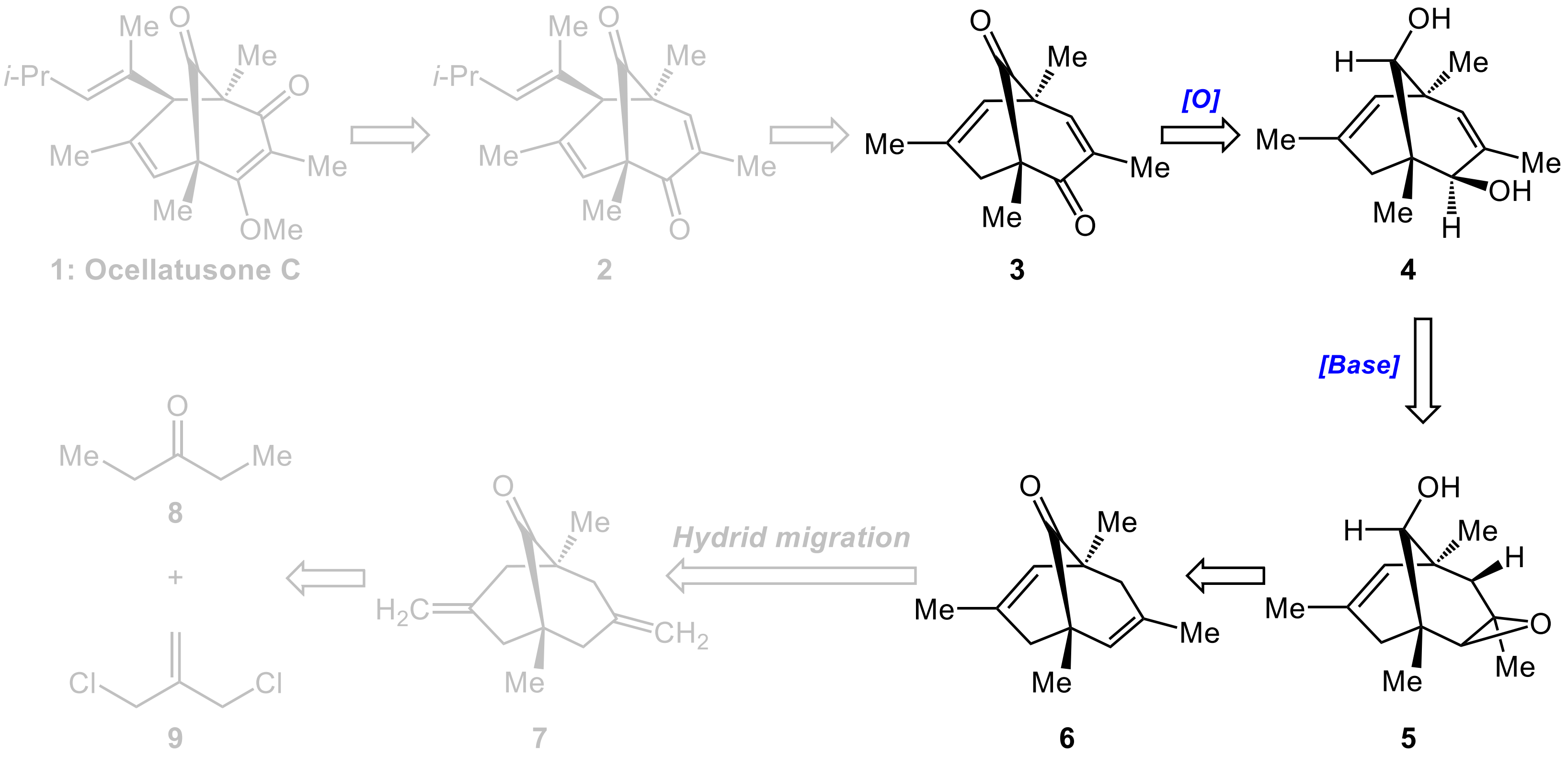
Synthesis of Intermediate 6



8 **9** **7** **6**



Retrosynthetic Analysis



1: Ocellatusone C

2

3

4

5

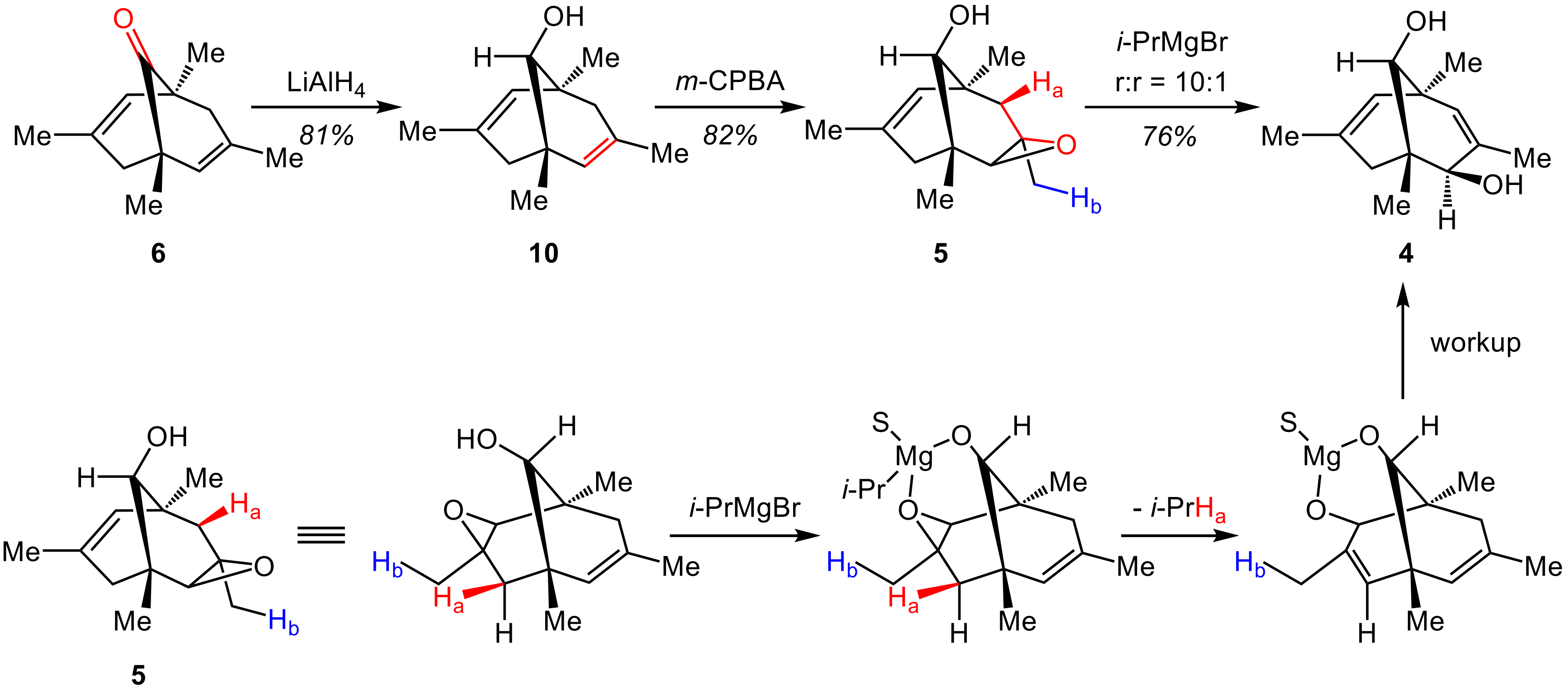
6

7

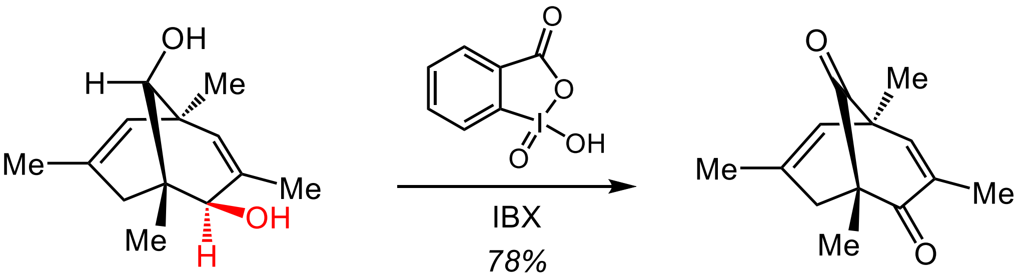
8

9

Synthesis of Intermediate 3



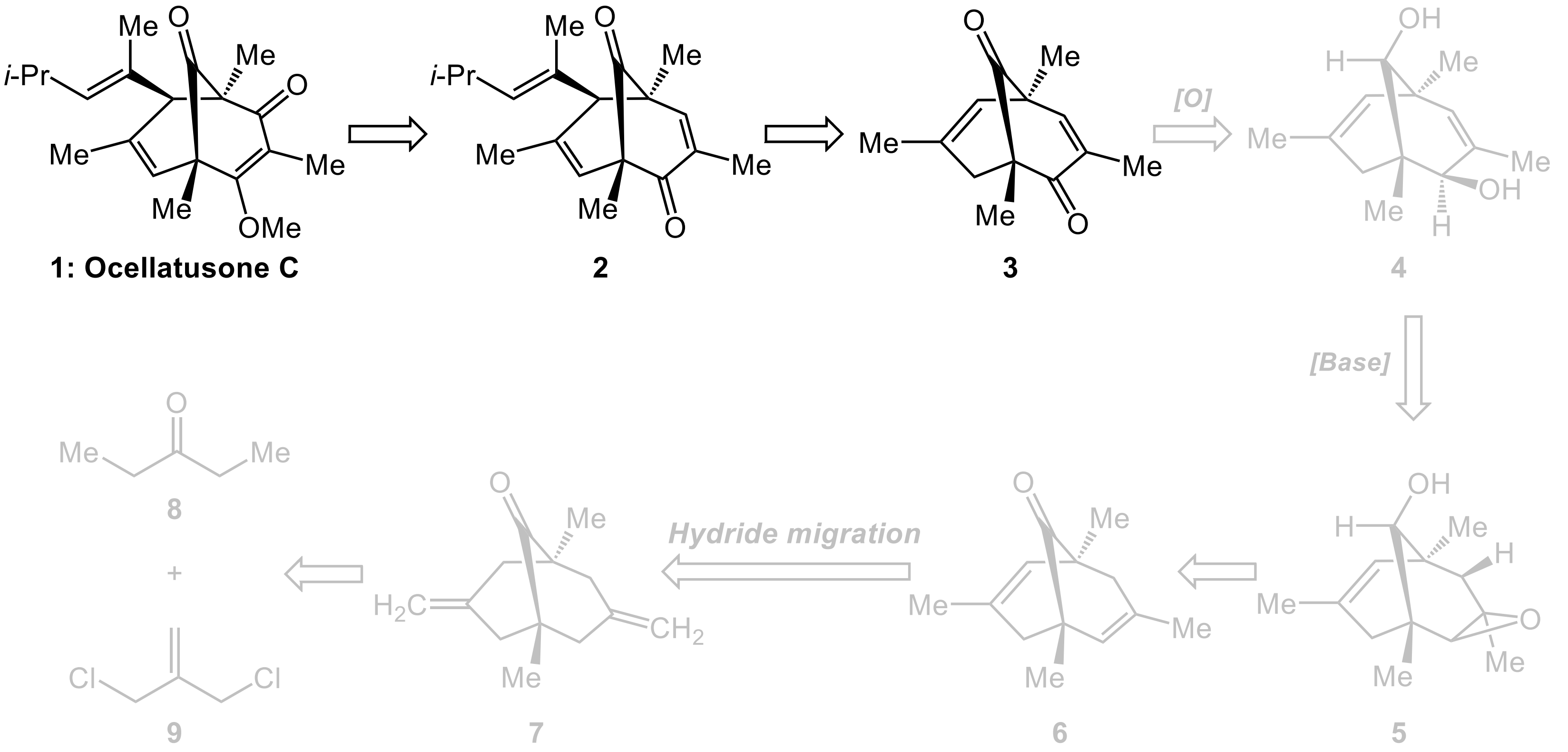
Synthesis of Intermediate 3



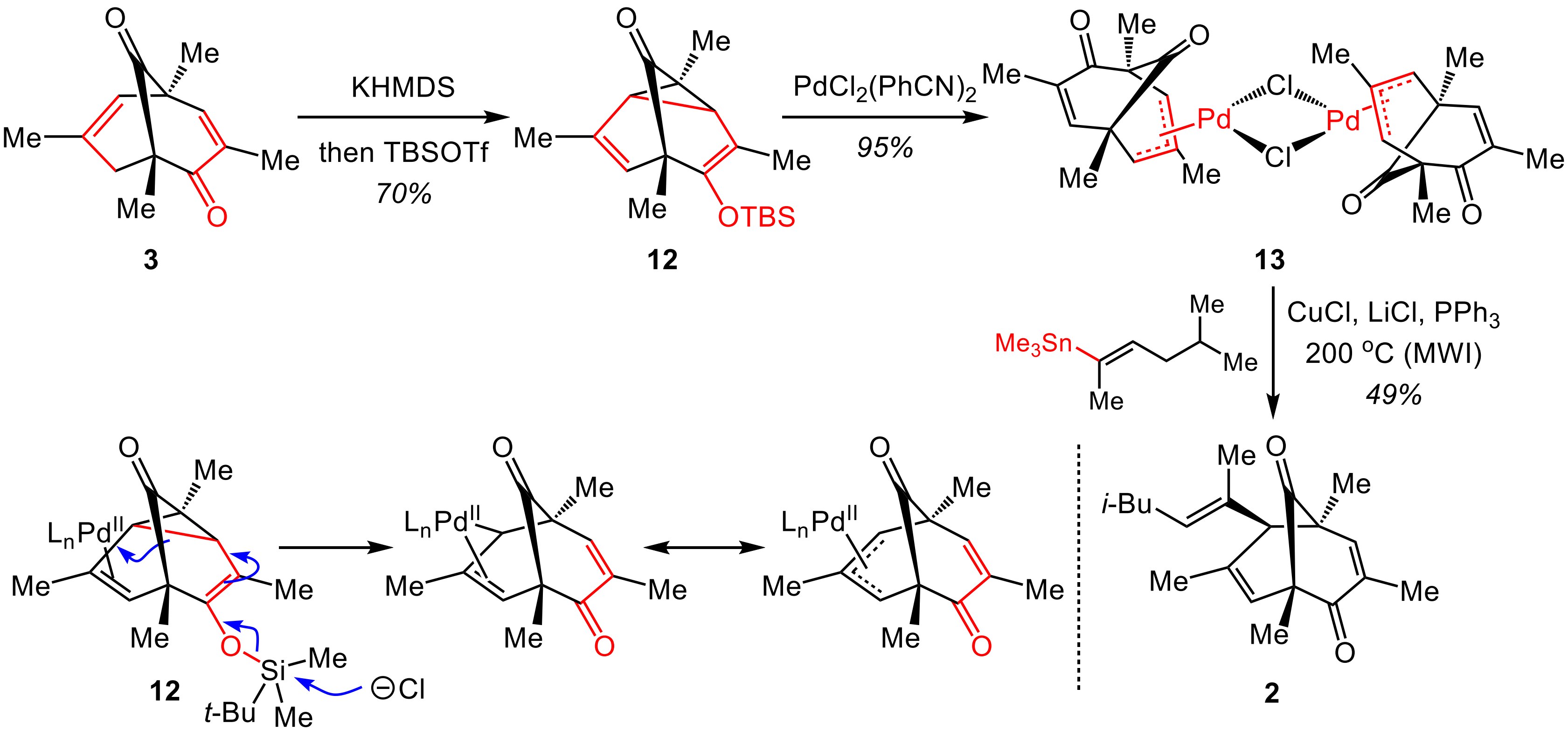
4

3

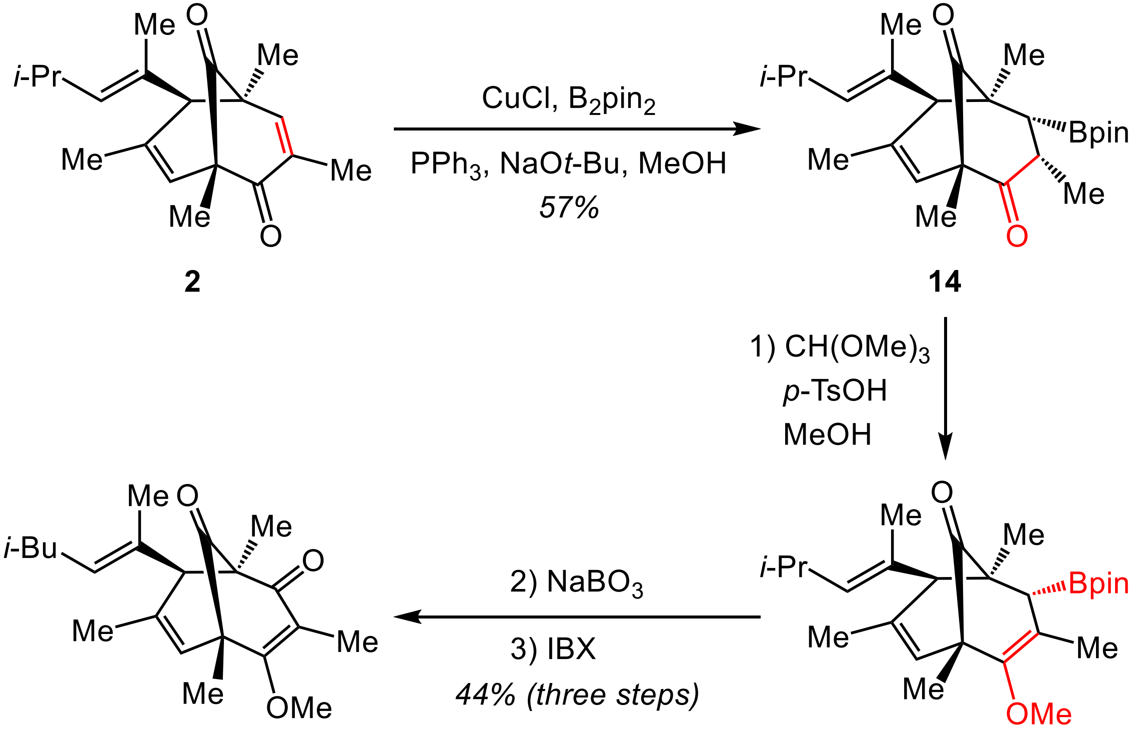
Retrosynthetic Analysis



Synthesis of Intermediate 2



Synthesis of Ocellatusone C



2

CuCl, B_2pin_2

PPh_3, NaO*t*-Bu, MeOH

57%

14

1) $CH(OMe)_3$

p-TsOH

MeOH

15

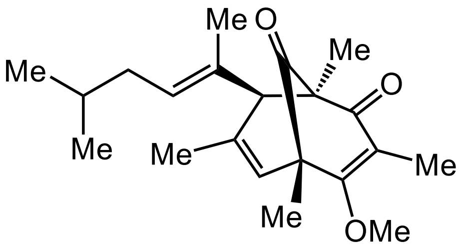
2) $NaBO_3$

3) IBX

44% (three steps)

1: Ocellatusone C

Summary



Ocellatusone C

13 steps
1.7% overall yield

- Pd-meditated hydride migration *(unsaturated [3.3.1]-bicycle);*
- π-allyl palladation *(dimeric π-allyl palladium complex);*
- Stille coupling reaction *(late-stage core functionalization).*

The First Paragraph

写作思路

分子结构和性质

常规合成思路

新型合成思路

The First Paragraph

Bridged bicyclononane carbon frameworks are a privileged structural motif found in over 1000 natural products−many with therapeutic relevance to human disease. Our research group has a longstanding interest in the synthesis of natural products containing the bridged bicyclo[3.3.1]nonane core. In this context, synthetic endeavors toward these molecular architectures have largely paralleled, or been inspired by, biosynthesis−often first installing substituents, and then constructing the core at a later stage.

The First Paragraph

Indeed, this synthetic blueprint has culminated in notable syntheses of many complex bicyclo[3.3.1]nonane-containing natural products. As a departure from this synthetic logic, we aimed to develop a divergent synthetic strategy to incorporate side chain fragments about the bicyclo-[3.3.1]nonane core at a late stage. This approach presents an opportunity to explore structure−activity relationships (SARs) of complex bicyclo-[3.3.1]nonanes by varying side chains from a common core intermediate potentially at a late stage.

The Last Paragraph

写作思路

总结成果

↓

阐述意义

The Last Paragraph

In summary, a synthetic blueprint rooted in late-stage diversification of a bicyclo[3.3.1]nonane framework has enabled the discovery, study, and facile synthesis of unusual shapeshifting anions and their complexation with transition metals. As a proving ground, the reactivity of these intermediates was leveraged to enable the concise synthesis of ocellatusone C. These shapeshifting intermediates relate highly substituted bicyclo[3.3.1] and [3.2.2]nonane frameworks via a common barbaralyl nucleus, a feature which may prove useful in the synthesis of other bridged bicyclononane-containing natural products and fluxional molecules. Finally, this work highlights the power of complex molecule synthesis to guide the discovery and exploration of new reactive intermediates in organic chemistry.

Representative Examples

- Our research group has a longstanding interest in the synthesis of natural products containing the bridged bicyclo[3.3.1]nonane core.

  (阐述课题组研究方向)

- Indeed, this synthetic blueprint has culminated in notable syntheses of many complex bicyclo[3.3.1]nonane-containing natural products.

  (表明某项方法成熟)

- Finally, this work highlights the power of complex molecule synthesis to guide the discovery and exploration of new reactive intermediates in organic chemistry. (强调某项工作意义)

Acknowledgement

Thanks for your attention