

Literature Report VII

Total Synthesis of (+)-Randainin D

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Checker: Yu-Qing Bai

Vyhivskyi, O.; Baudoin, O.* *J. Am. Chem. Soc.* **2024**, *146*, 11486.

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CV of Prof. Olivier Baudoin



Background:

- ❑ **1992-1995** B.S., Ecole Nationale Supérieure de Chimie de Paris
- ❑ **1995-1998** Ph.D., Collège de France
- ❑ **1999** Postdoc., Scripps Research Institute
- ❑ **1999-2006** Group Leader and CNRS “Chargé de Recherche”, Institut de Chimie des Substances Naturelles
- ❑ **2006-2015** Full Professor, Université Claude Bernard Lyon 1
- ❑ **2015-now** Full Professor, University of Basel

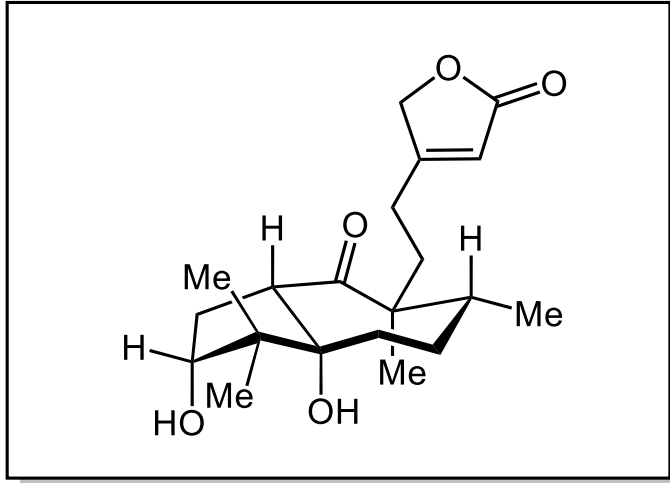
Research:

- Functionalization of C–H bonds;
- Synthesis of natural products.

Contents

- 1** Introduction
- 2** Total Synthesis of Diterpene (+)-Randainin D
- 3** Summary

Introduction



(+)-Randainin D

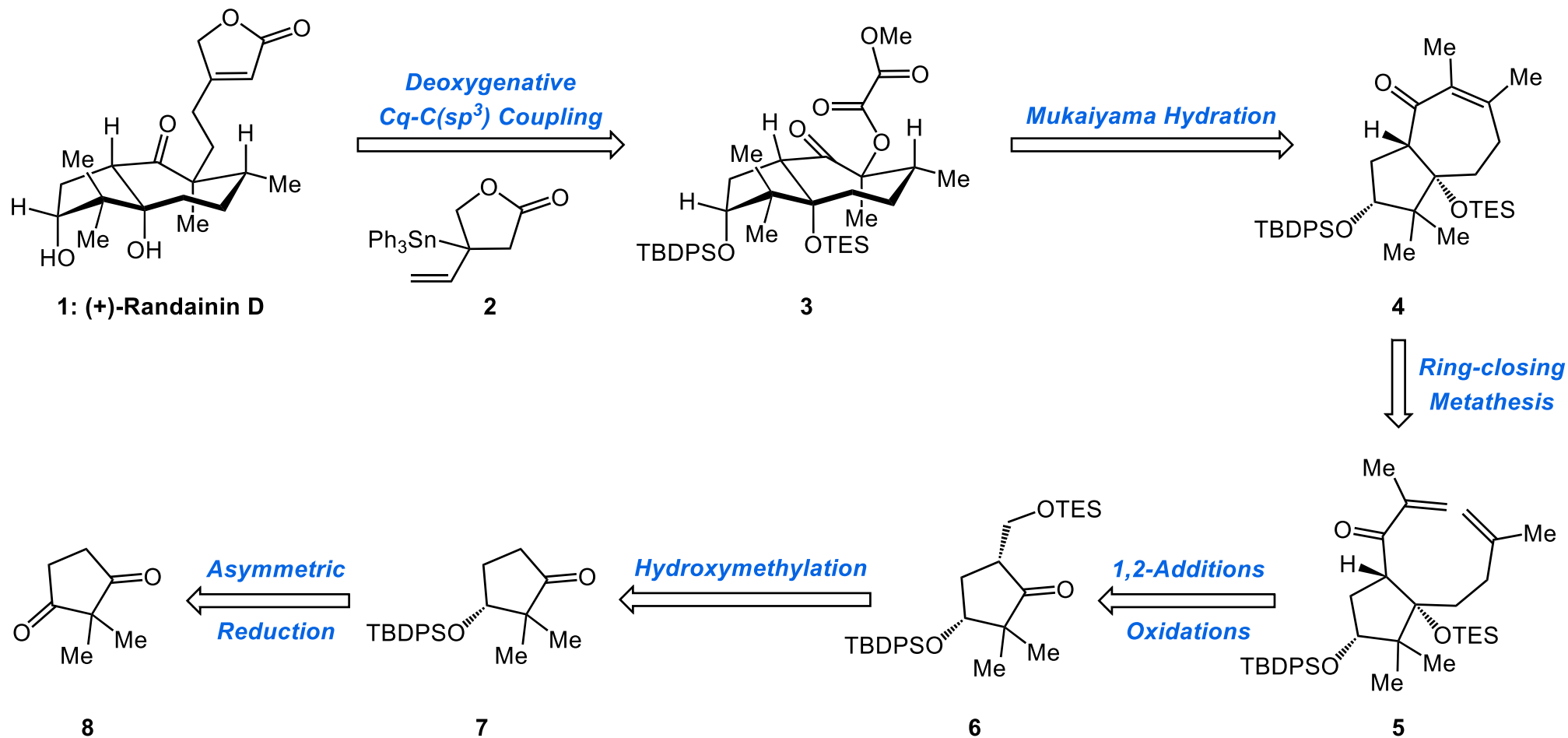


Callicarpa randaiensis

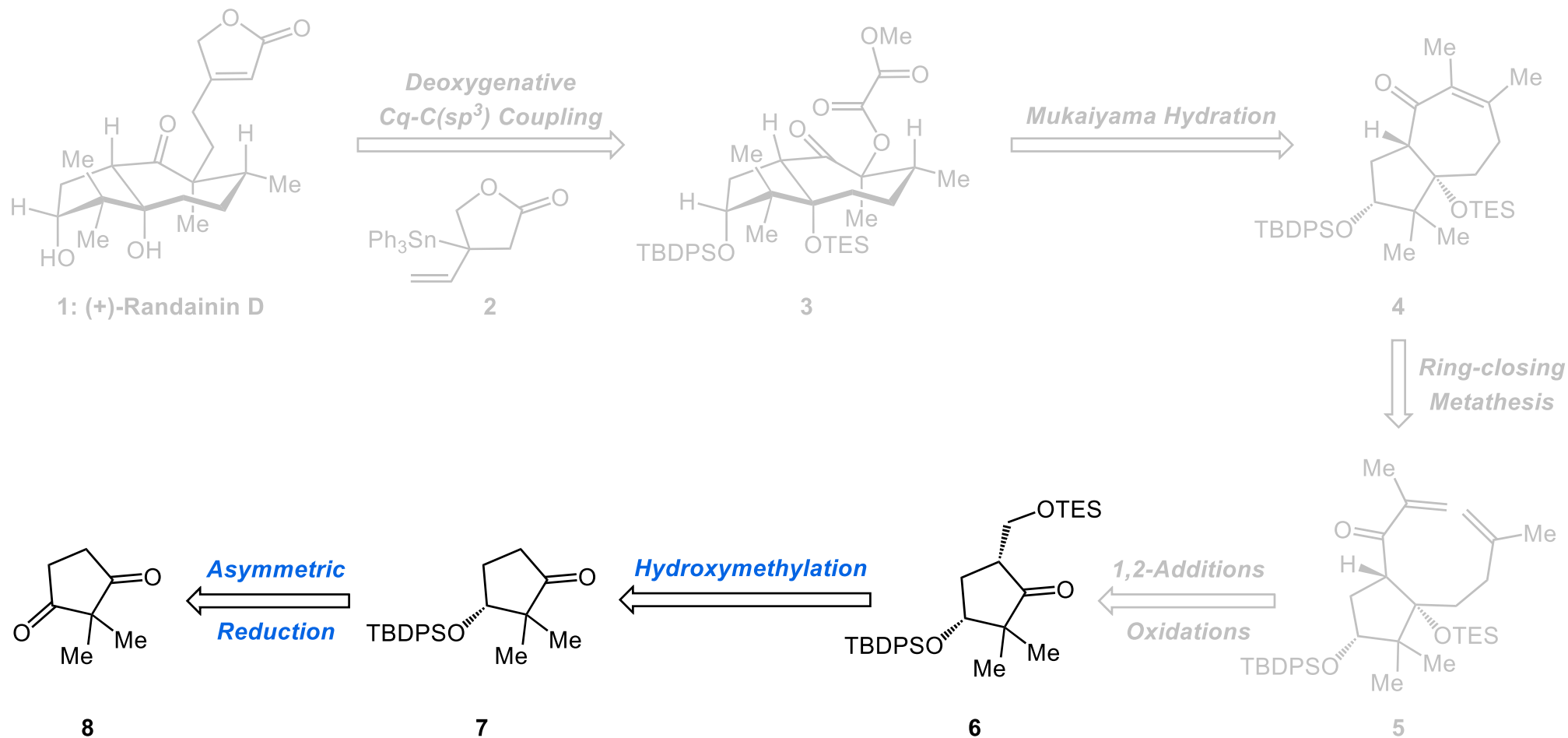
- It was isolated from the leaves and twigs of *Callicarpa randaiensis* in 2015;
- It contains a unusual *trans*-5/7 ring scaffold with 5 stereogenic centers (1 quaternary);
- Bioassays show that it inhibits elastase release, which suggests the therapeutic potential in the treatment of COVID-19.

Chen, H.-H.; Cheng, Y.-B.; Hwang, T.-L.; Kuo, Y.-H.; Chen, C.-H.; Shen, Y.-C.* *J. Nat. Prod.* **2015**, 78, 1823

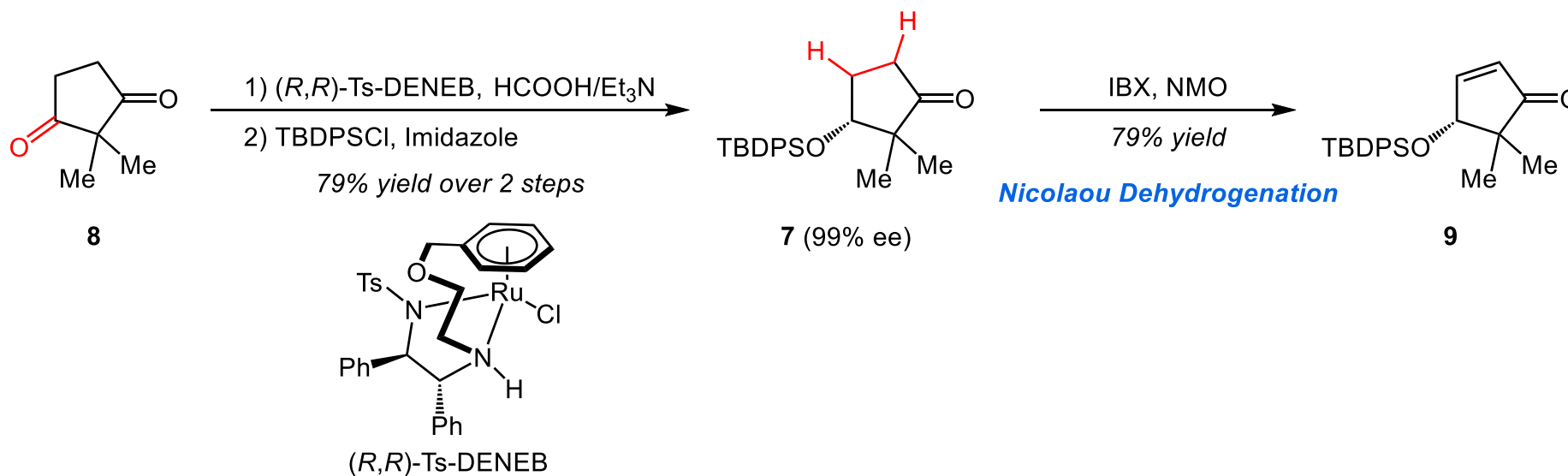
Retrosynthetic Analysis



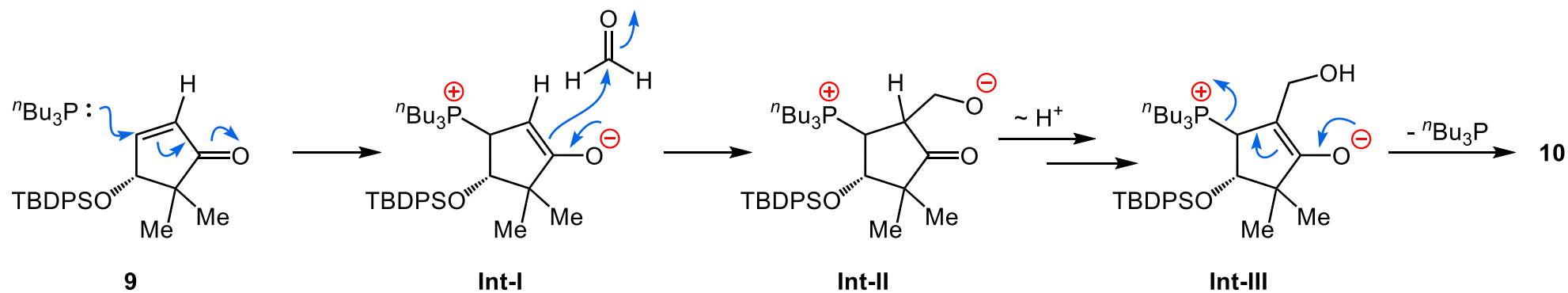
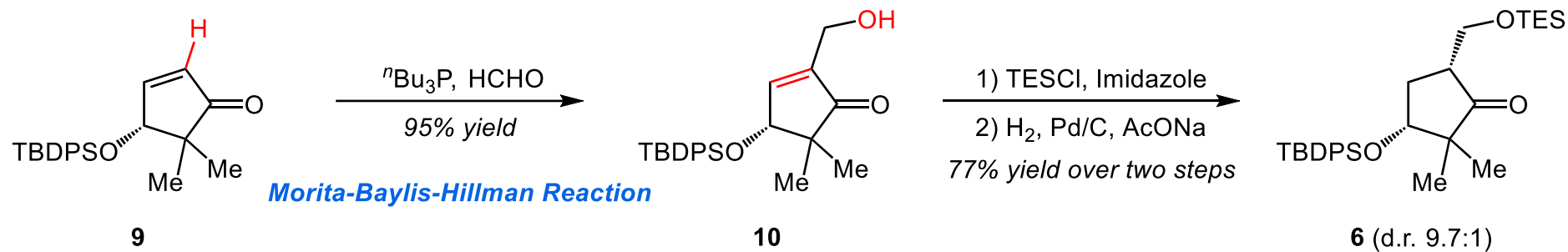
Retrosynthetic Analysis



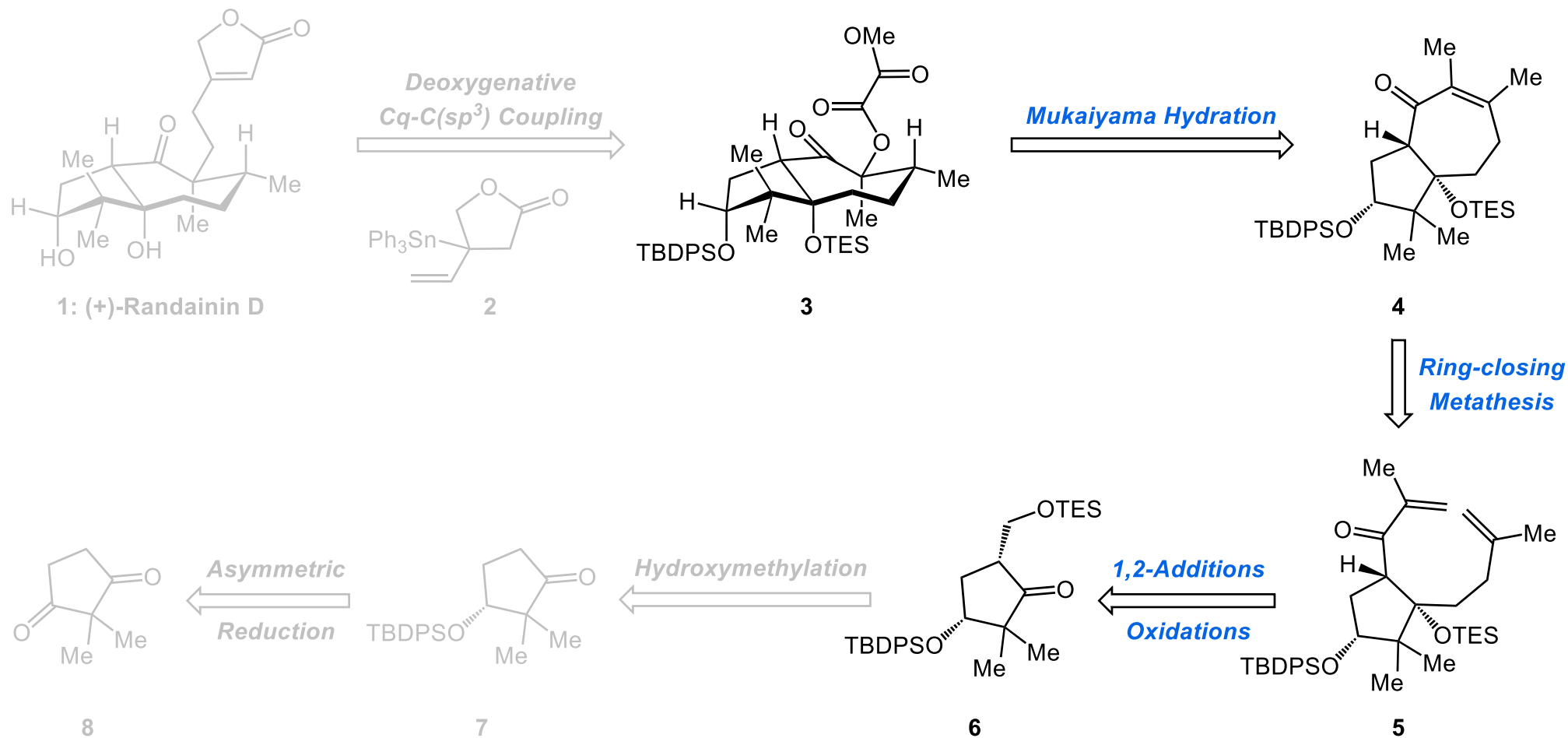
Synthesis of Compound 9



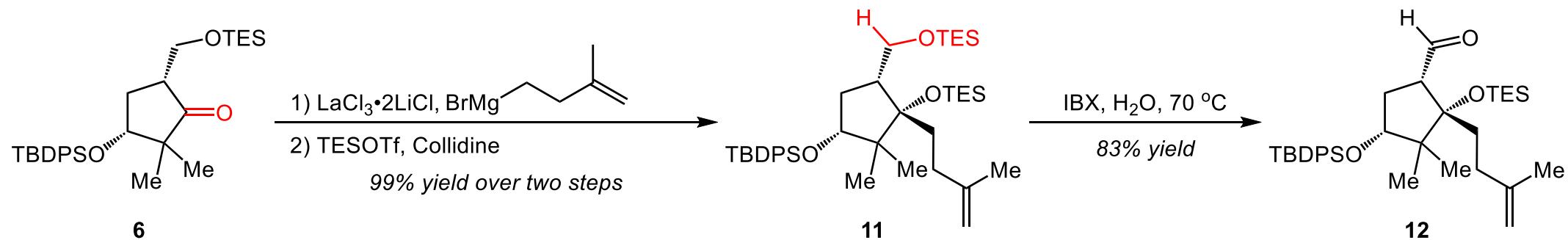
Synthesis of Compound 6



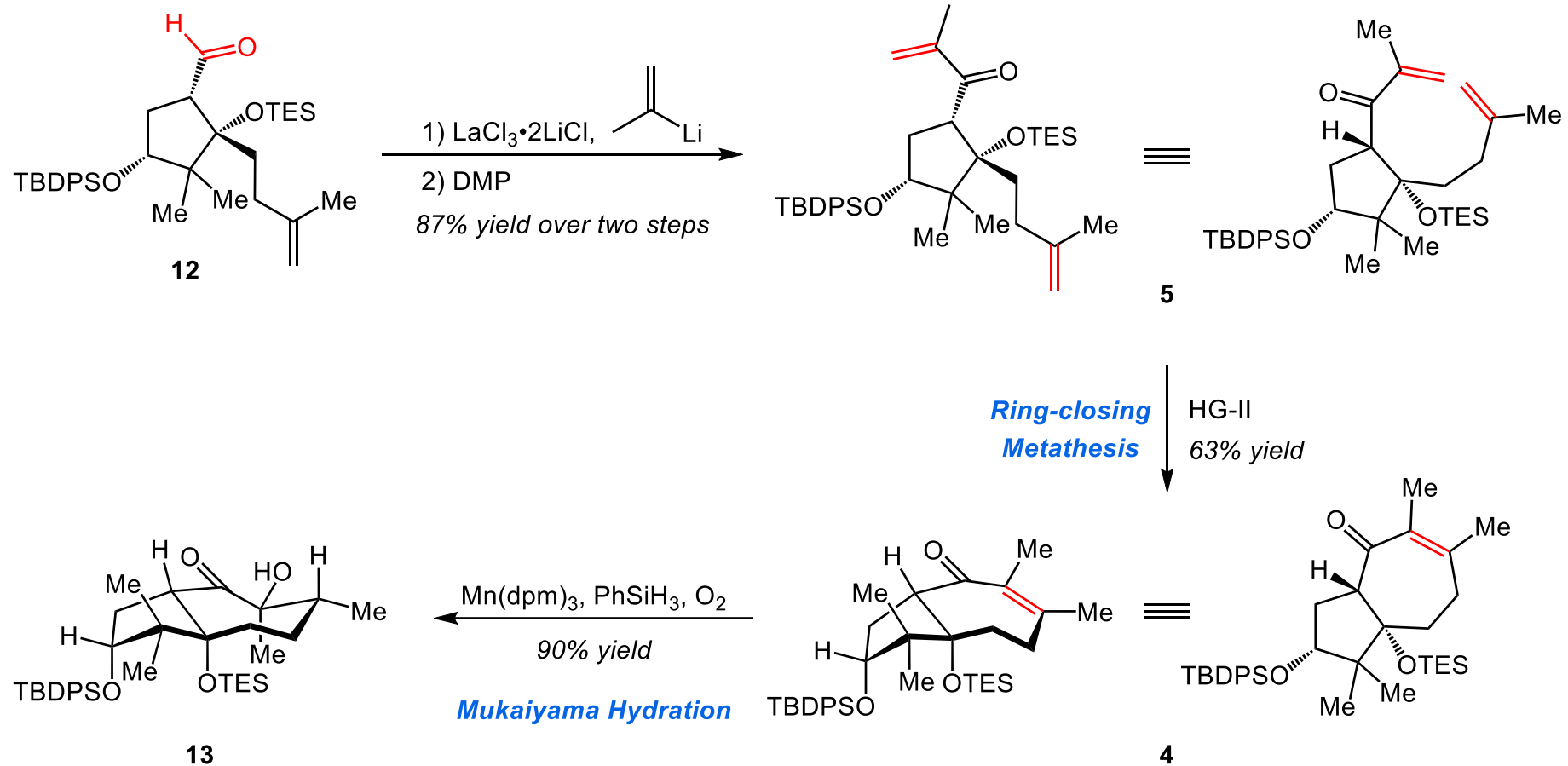
Retrosynthetic Analysis



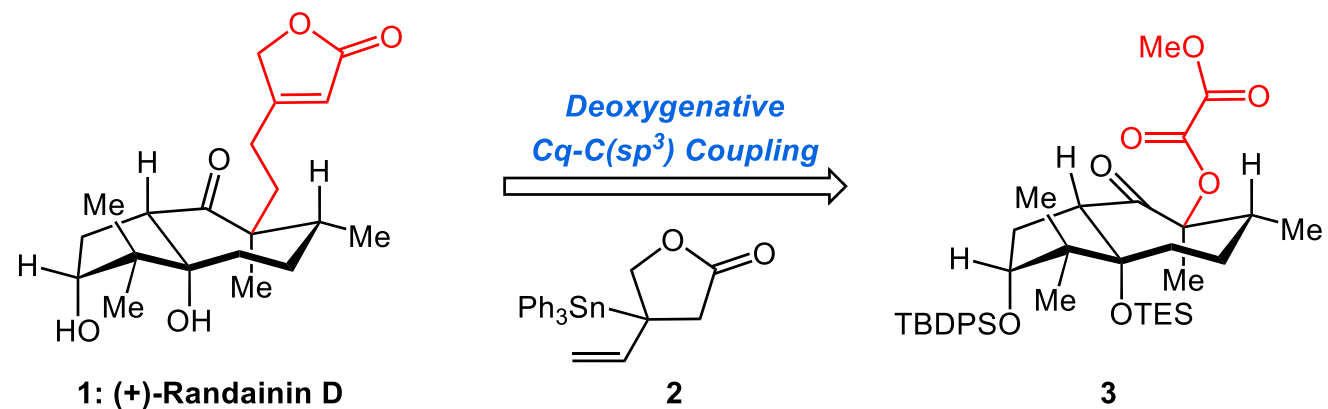
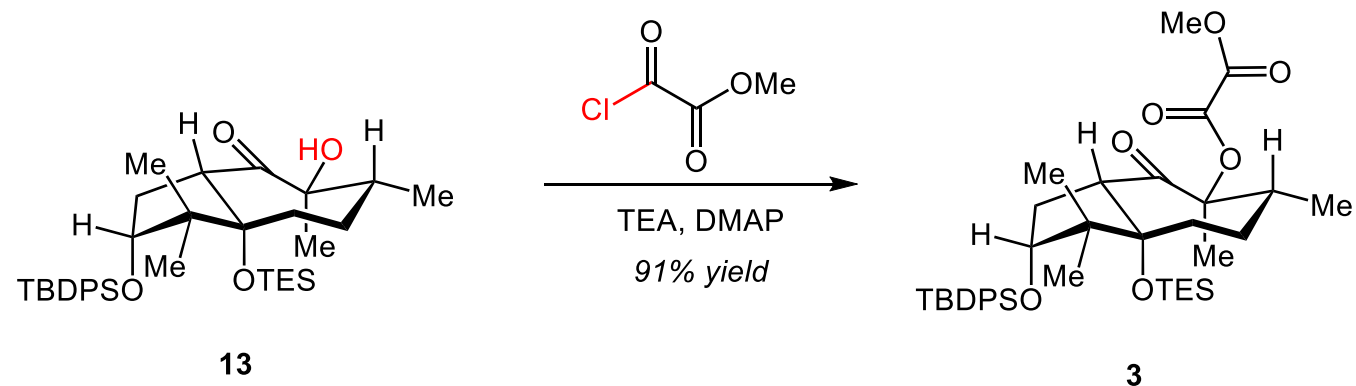
Synthesis of Compound 12



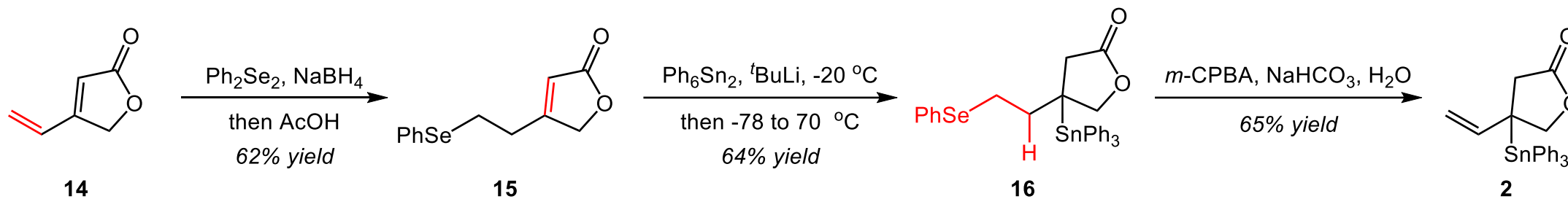
Synthesis of Compound 13



Synthesis of Compound 3

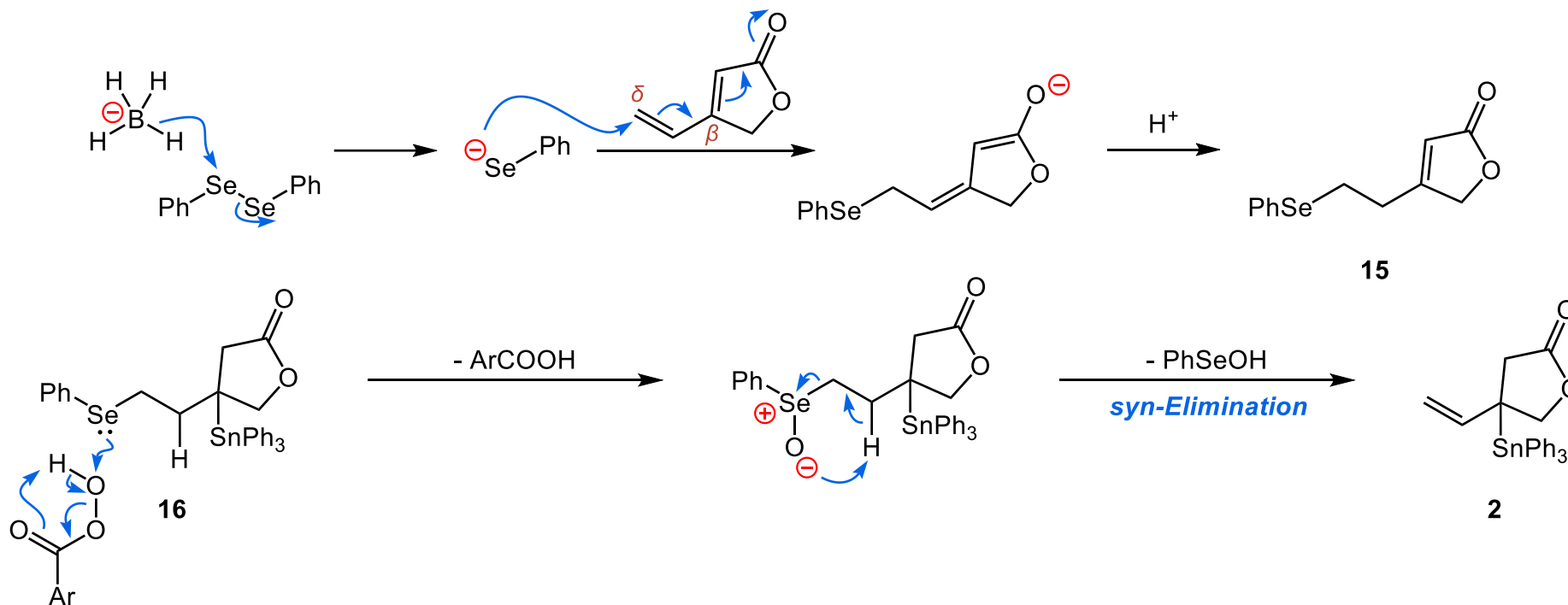


Synthesis of Compound 2

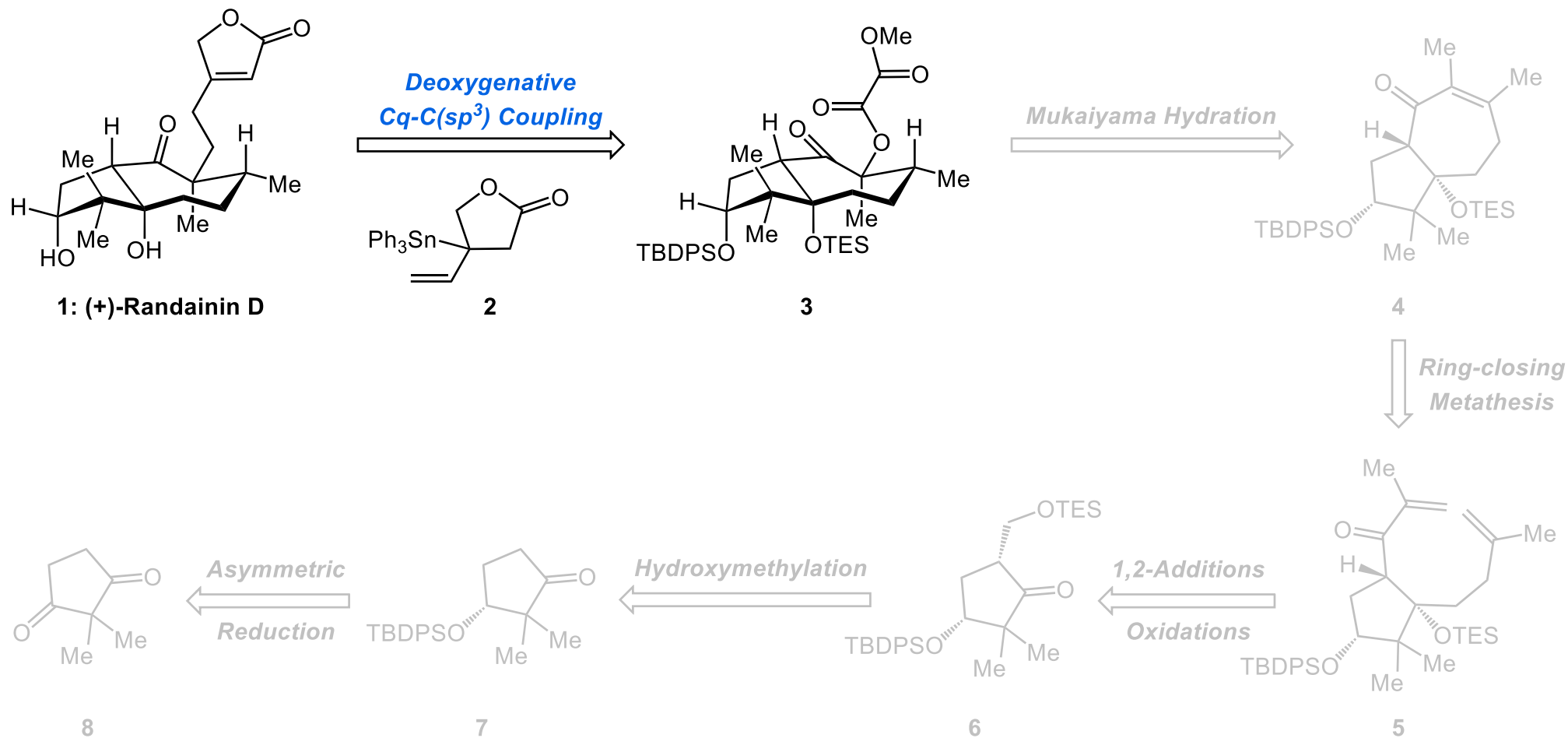


Protection

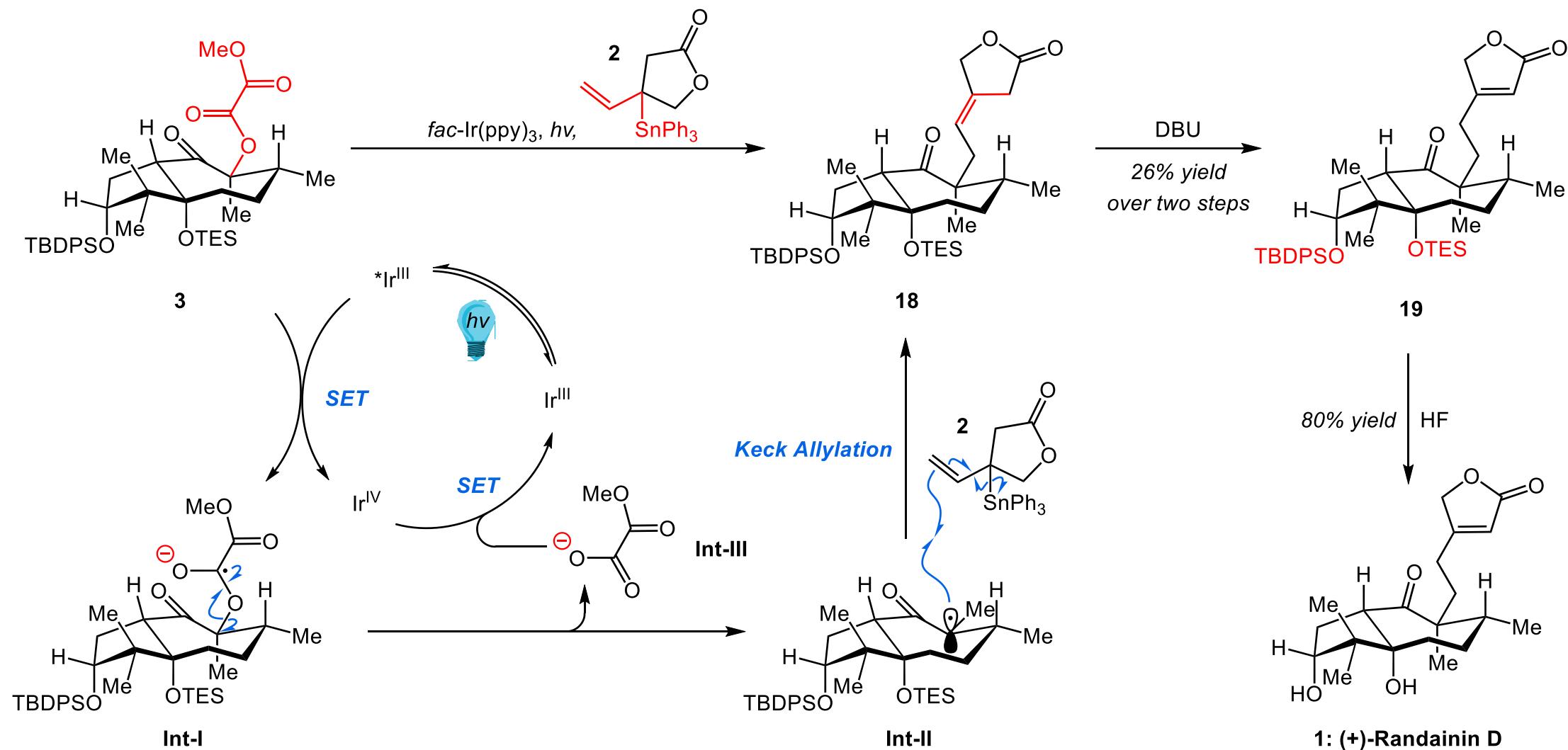
Deprotection



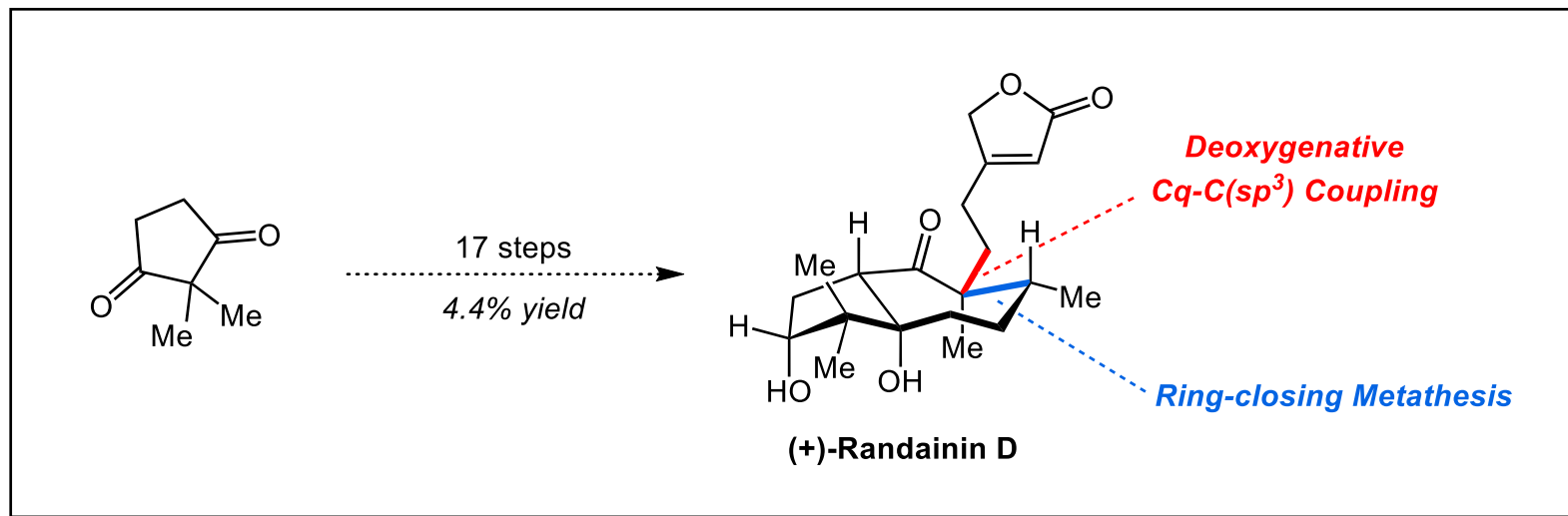
Retrosynthetic Analysis



Synthesis of Compound Diterpene (+)-Randainin D



Summary



- Ring-closing Metathesis (construction of *trans*-5/7 ring scaffold);
- Deoxygenative Cq-C(sp³) Coupling (assembly of fragments).

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Writing Strategy

➤ First paragraph

Species and
Physiological Activity



The significance of
total synthesis

- Terpenoids are the vastest family of natural products, accounting for over 80,000 unique compounds. The terpenome ubiquity and diversity are accompanied by a wide range of bioactivities, including anticancer, anti-inflammatory, anticoagulative, sedative, and antioxidative effects.
- The interesting biological properties of terpenoids, combined with the complexity of the structures, have led to a myriad of total syntheses that both contribute to solving current synthetic issues in organic chemistry and to advance the search for new therapeutic agents.

Writing Strategy

➤ Last paragraph

Summary

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graph TD; A[Summary] --> B[Committed Steps]; B --> C[Prospect];
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Committed Steps

Prospect

- In conclusion, we have completed the first enantioselective total synthesis of the diterpene (+)-randainin D (17 steps) ...
- Key to these syntheses was the combination of RCM of substituted enones with a novel Ir^{III}-photocatalyzed deoxygenative allylation. This study expands the toolbox of synthetic strategies for the construction of polycyclic systems bearing *trans*-cycloheptane scaffolds including complex terpenoids.
- Additionally, it features an innovative approach for the late stage incorporation of the β -substituted butenolide moiety, found in numerous natural products.

Representative Examples

- The interesting biological properties of terpenoids, combined with the complexity of the structures, have led to **a myriad of** total syntheses that both contribute to solving current synthetic issues in organic chemistry and to advance the search for new therapeutic agents. (无数的, 大量的)
- **Global deprotection** of the silyl groups with aqueous HF in CH₃CN afforded (+)-randainin D (**3**), the physicochemical properties of which fully matched those reported. (全局去保护)
- **Admittedly**, the tetrasubstituted enone in **6** represents a significant challenge compared with previous cases. (诚然, 不可否认地)

Acknowledgement

Thank You for Your Attention

