Literature Report III

Ir-Catalyzed, Stereoselective Total Synthesis of (+)-Rubriflordilactone A

Reporter: Yu Yang
Checker: Hao-Dong Chen

Liu, J.-J.; Ni, Z.-B.; Li, L.; Yang, Y.-R. *J. Am. Chem. Soc.* **2025**, *147*, 16792

2025-09-01

CV of Prof. Yu-Rong Yang(杨玉荣)

Background:

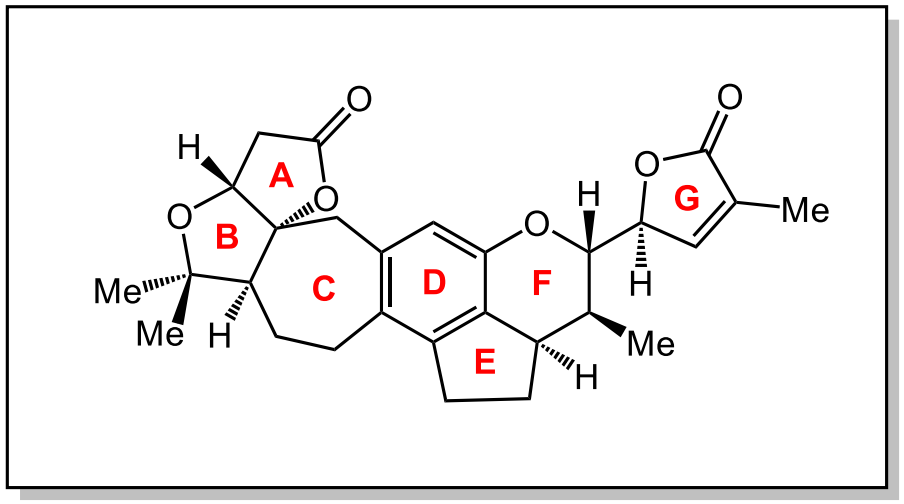
- **1996-2000** B. S., Lanzhou University
- **2000-2005** Ph. D., Lanzhou University
- **2005-2007** Postdoctor, Harvard University
- **2008-Now** Researcher, The Kunming Institute of Botany

Research Field:

- **Total Synthesis of Natural Products**
- **Organic Synthesis Methodology**

Contents

Introduction



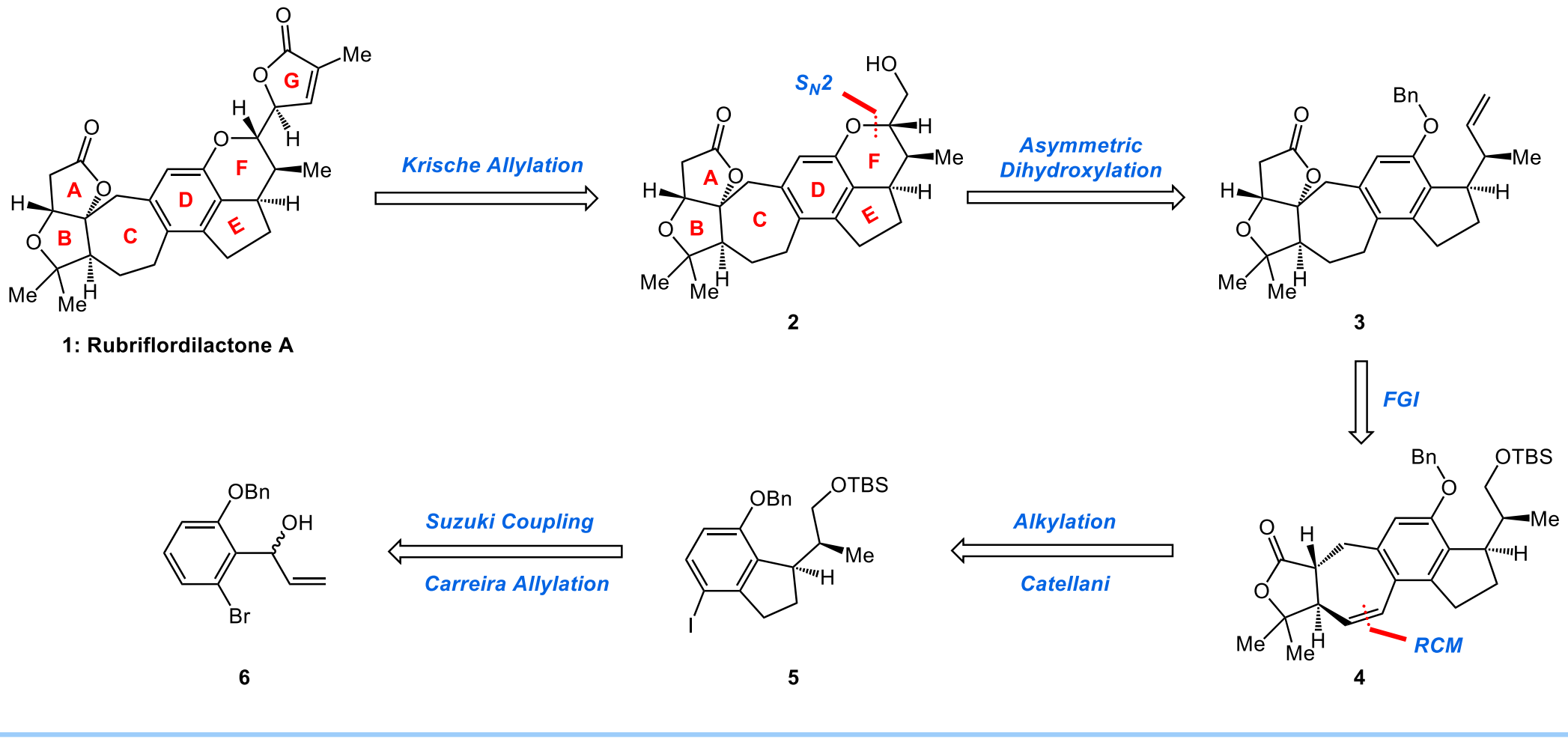
Rubriflordilactone *A*

Schisandra Chinensis

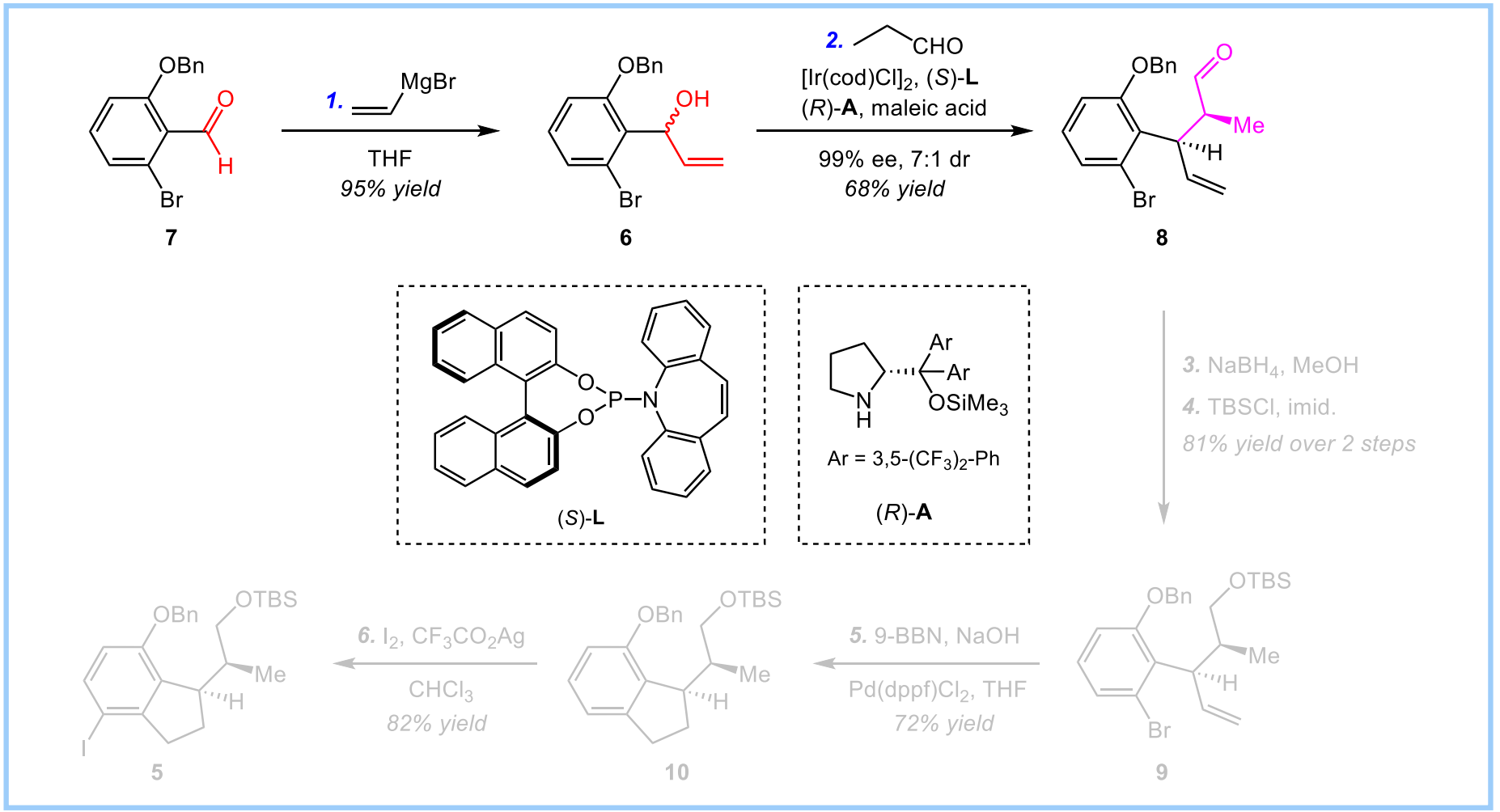
- It has been isolated from Schisandra species, primarily by Sun and colleagues;
- It is stereochemically dense and highly oxygenated polycyclic triterpenoids;
- Bioassays showed that it possessed anti-inflammatory and anti-HIV-1 activities.

Xiao, W.-L.; Yang, L.-M.; Gong, N.-B.; Wu, L.; Sun, H.-D. *Org. Lett.* **2006**, *8*, 991−994

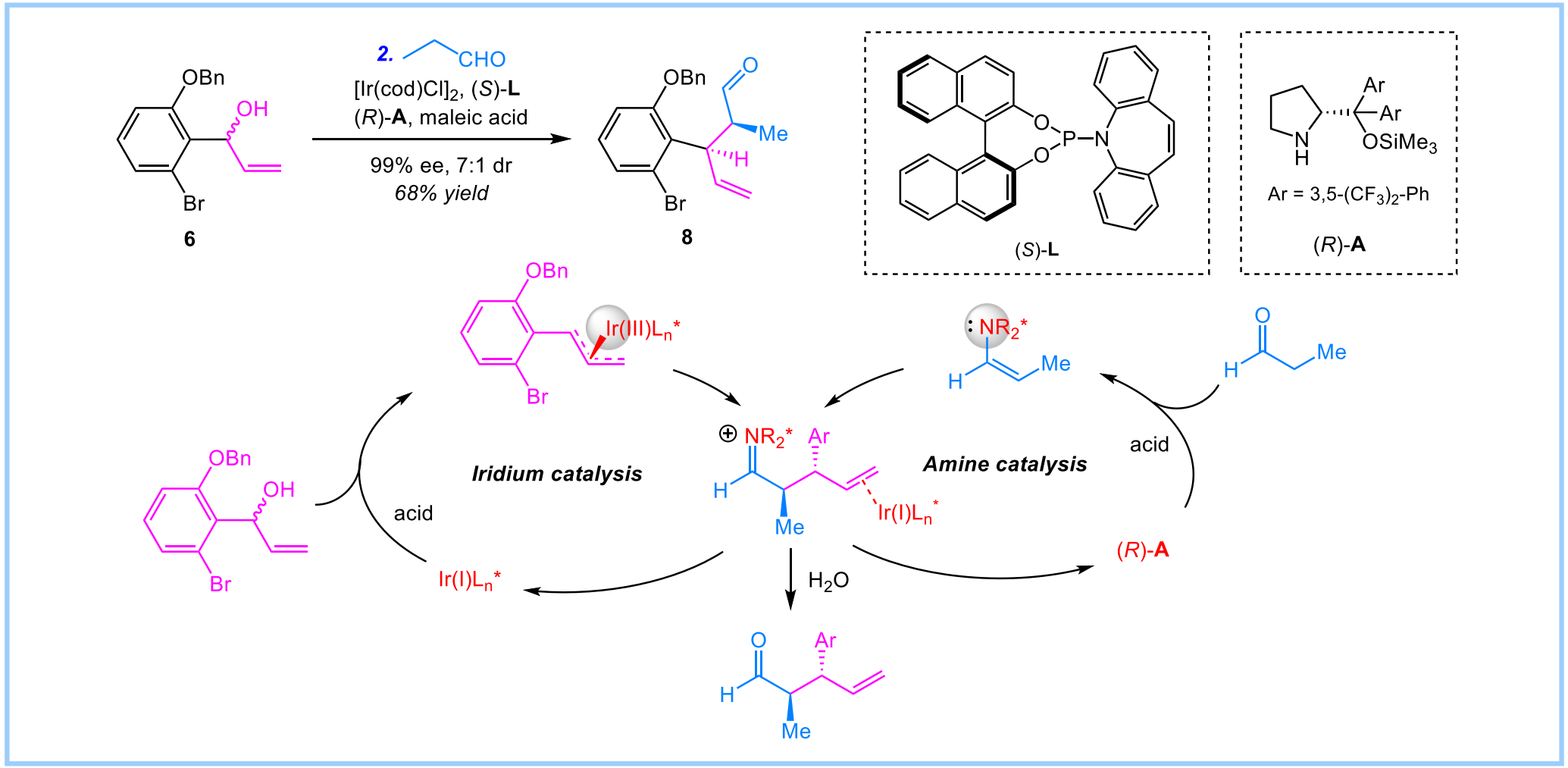
Retrosynthetic Analysis



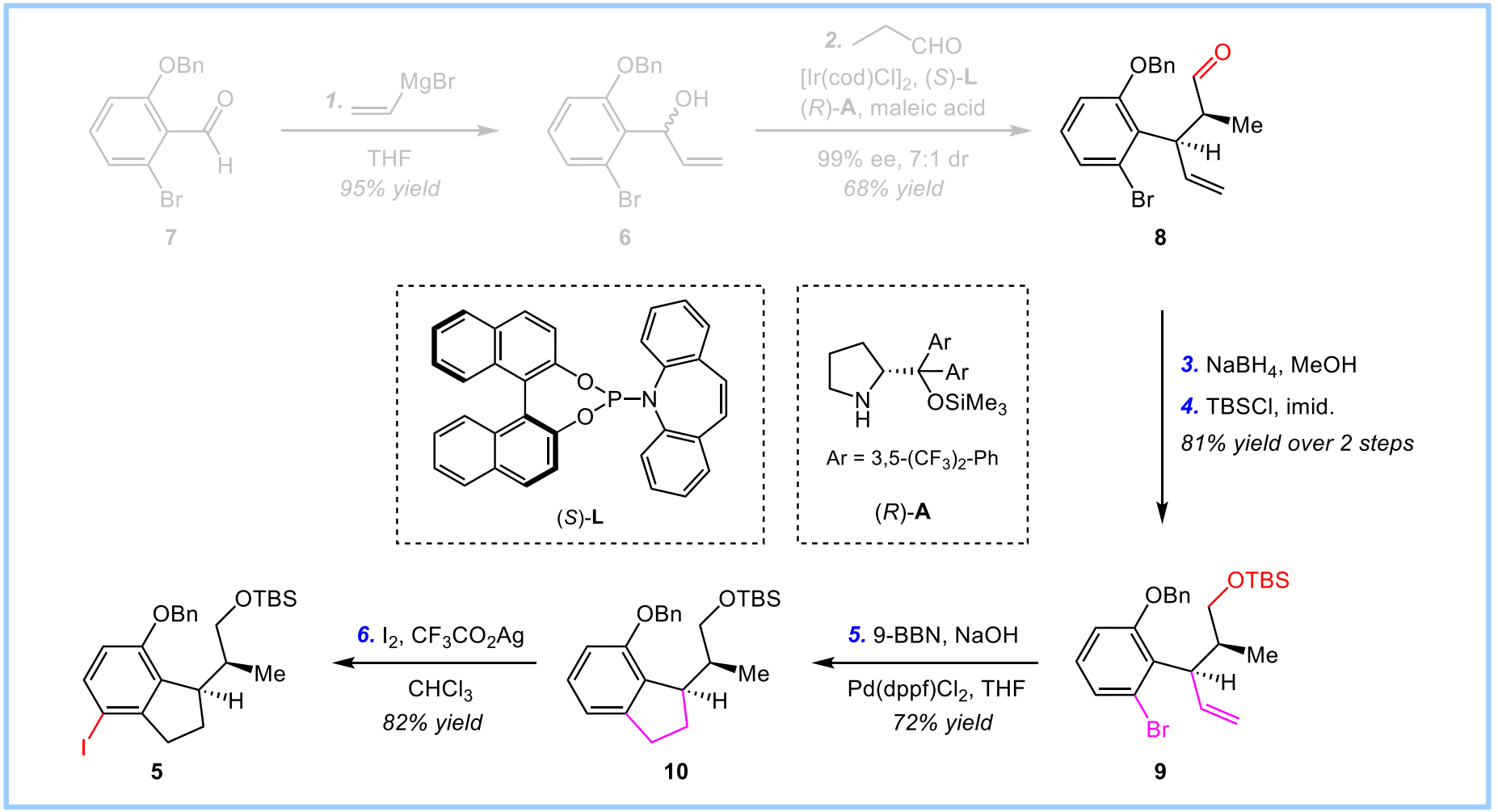
Synthesis of Compound 5



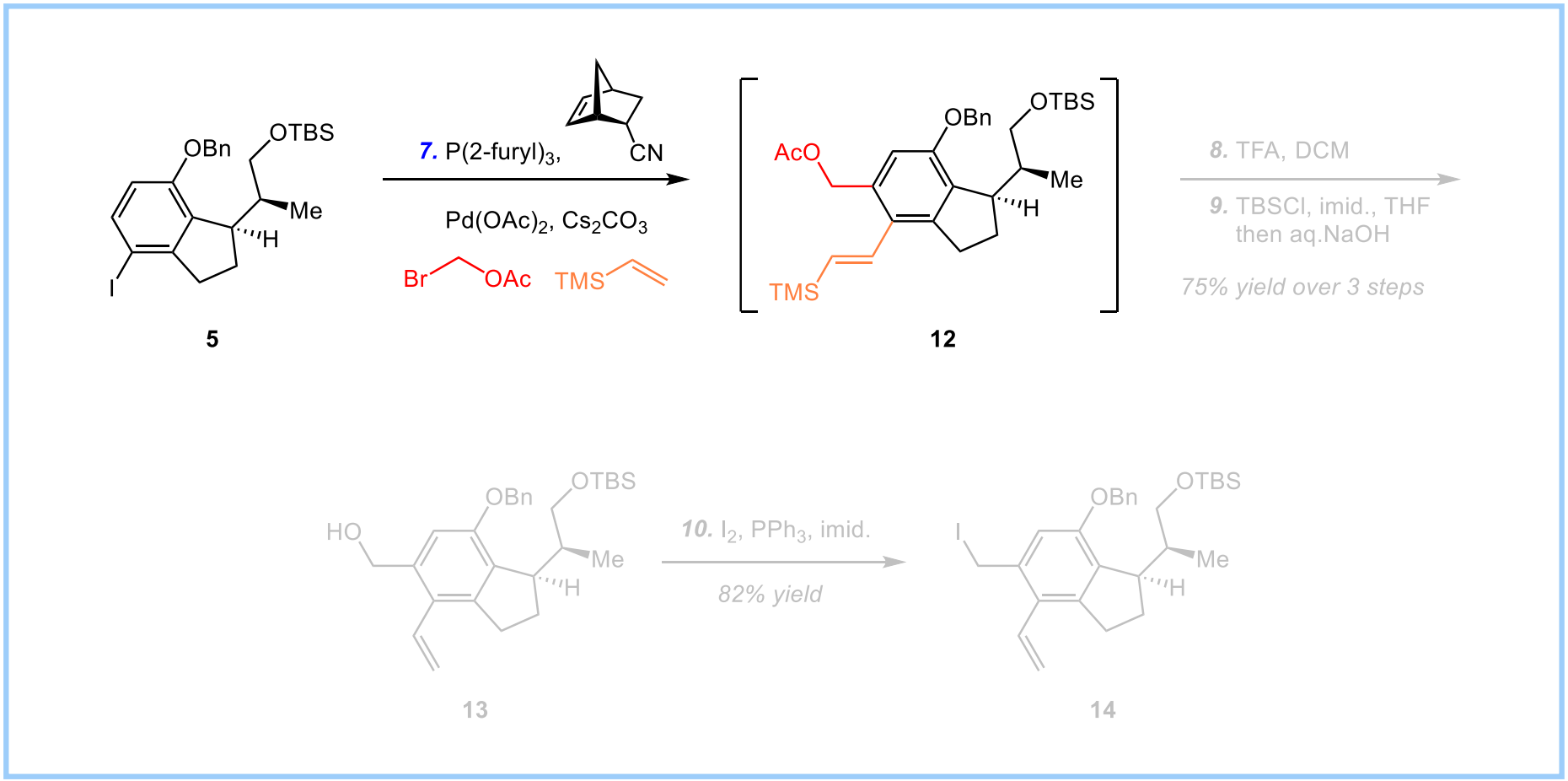
Carreira's Ir/Amine Dual-Catalyzed Allylation



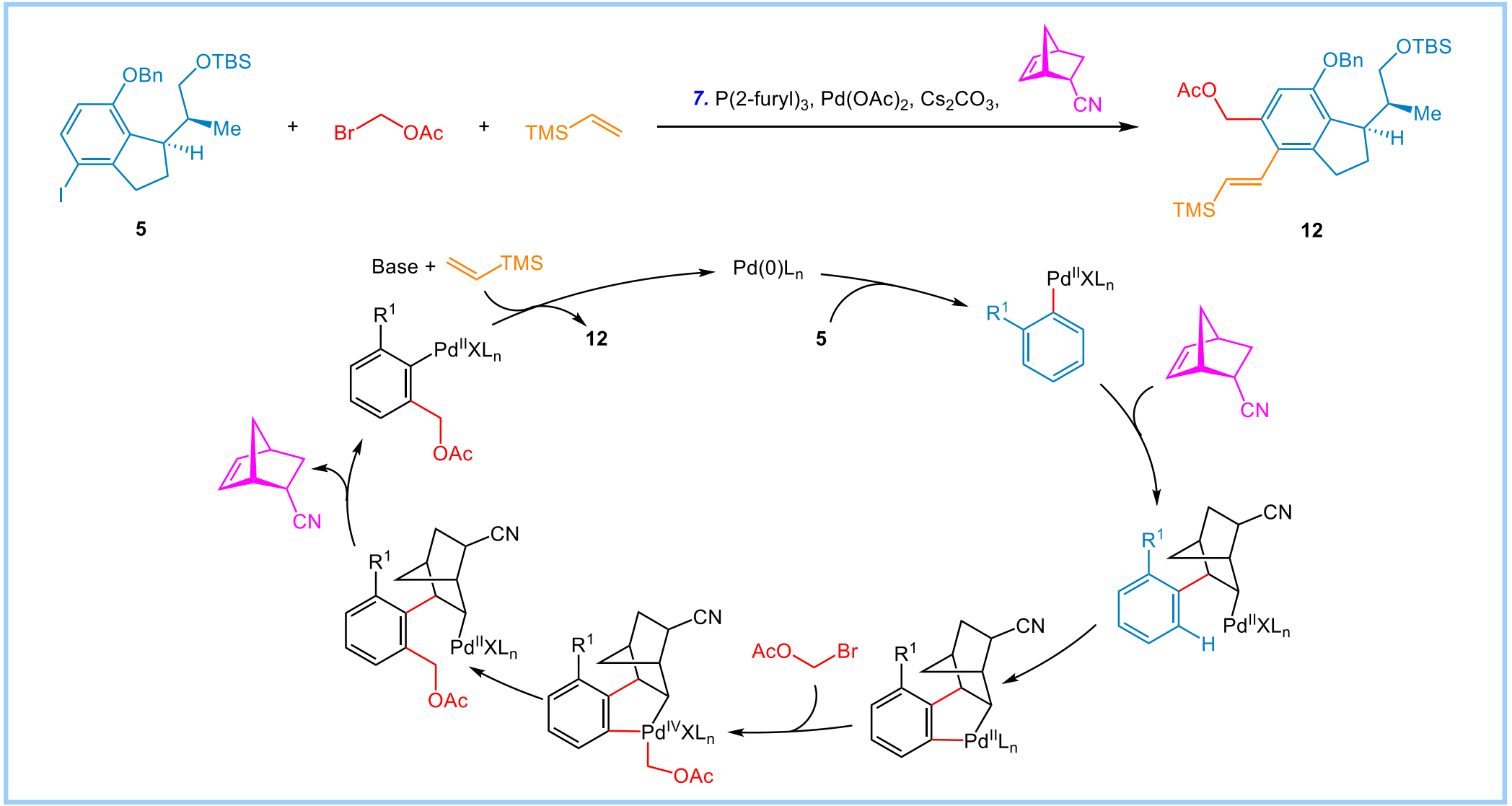
Synthesis of Compound 5



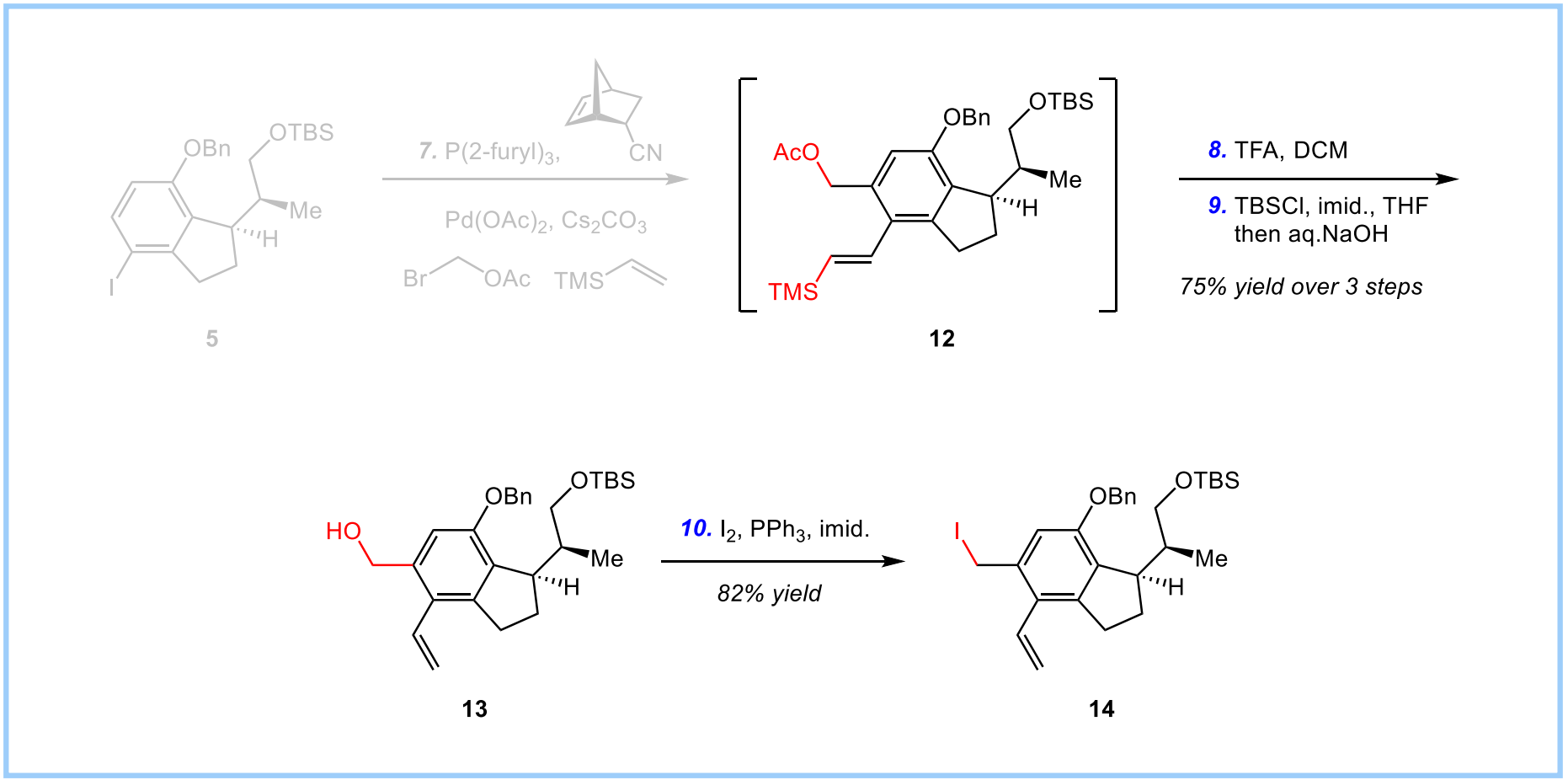
Synthesis of Compound 14



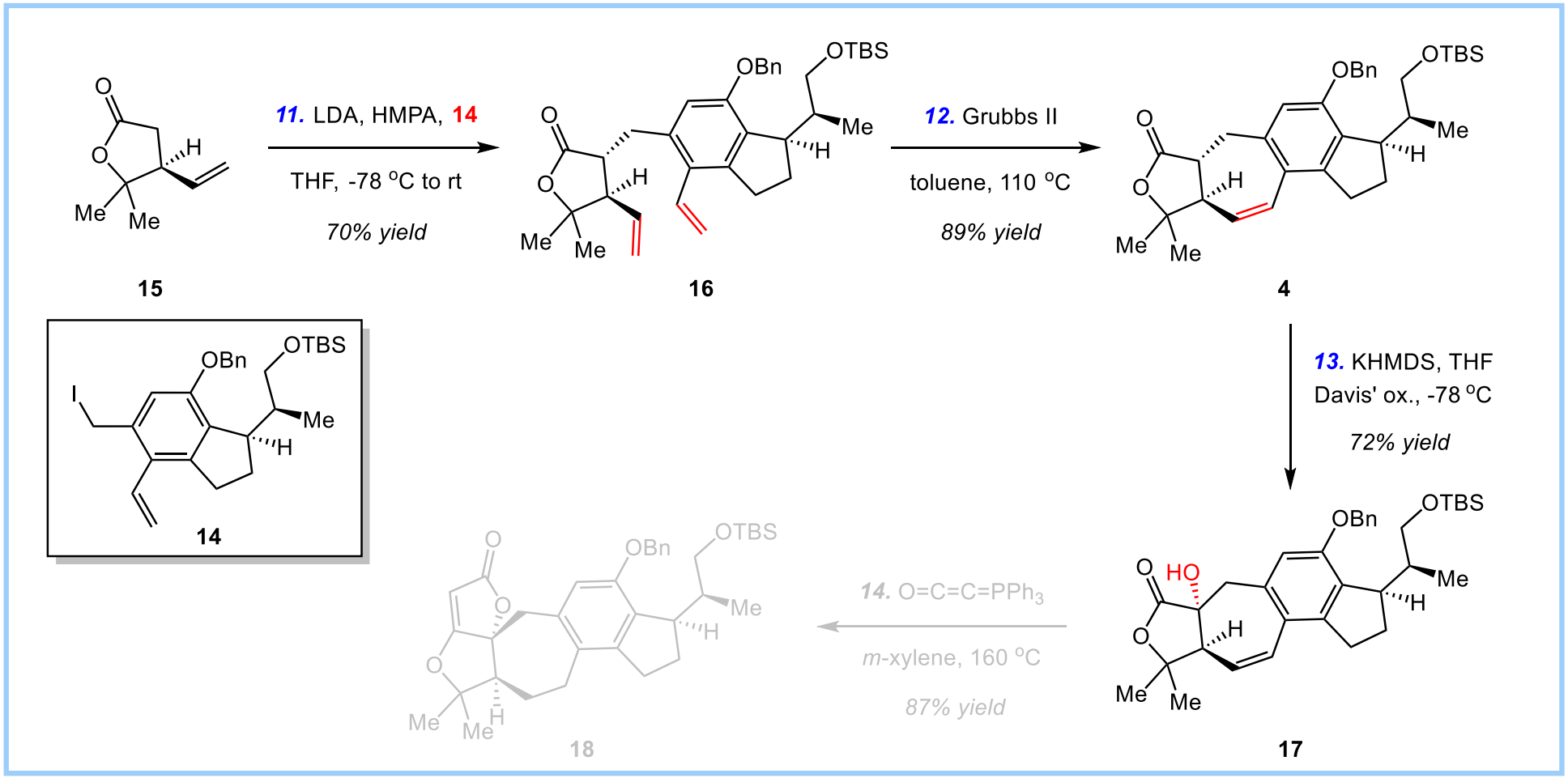
Catellani Reaction



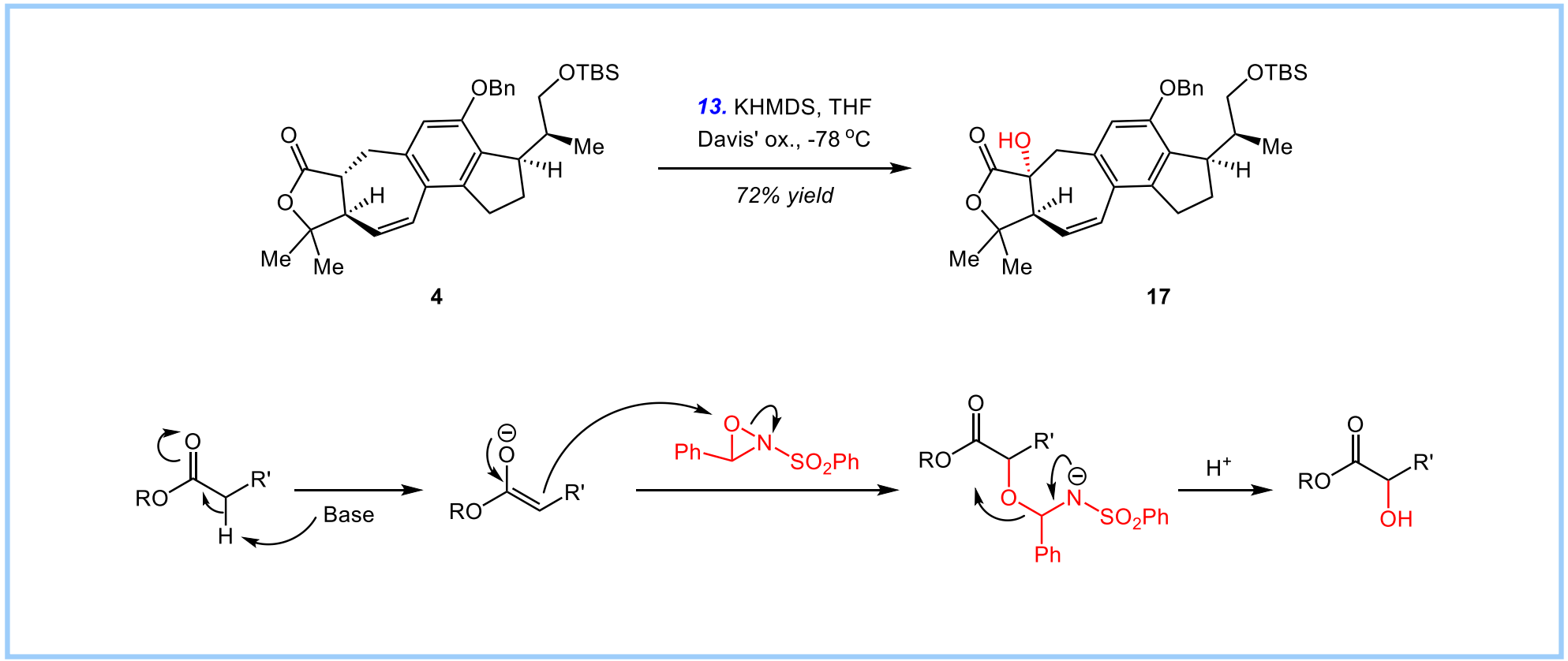
Synthesis of Compound 14



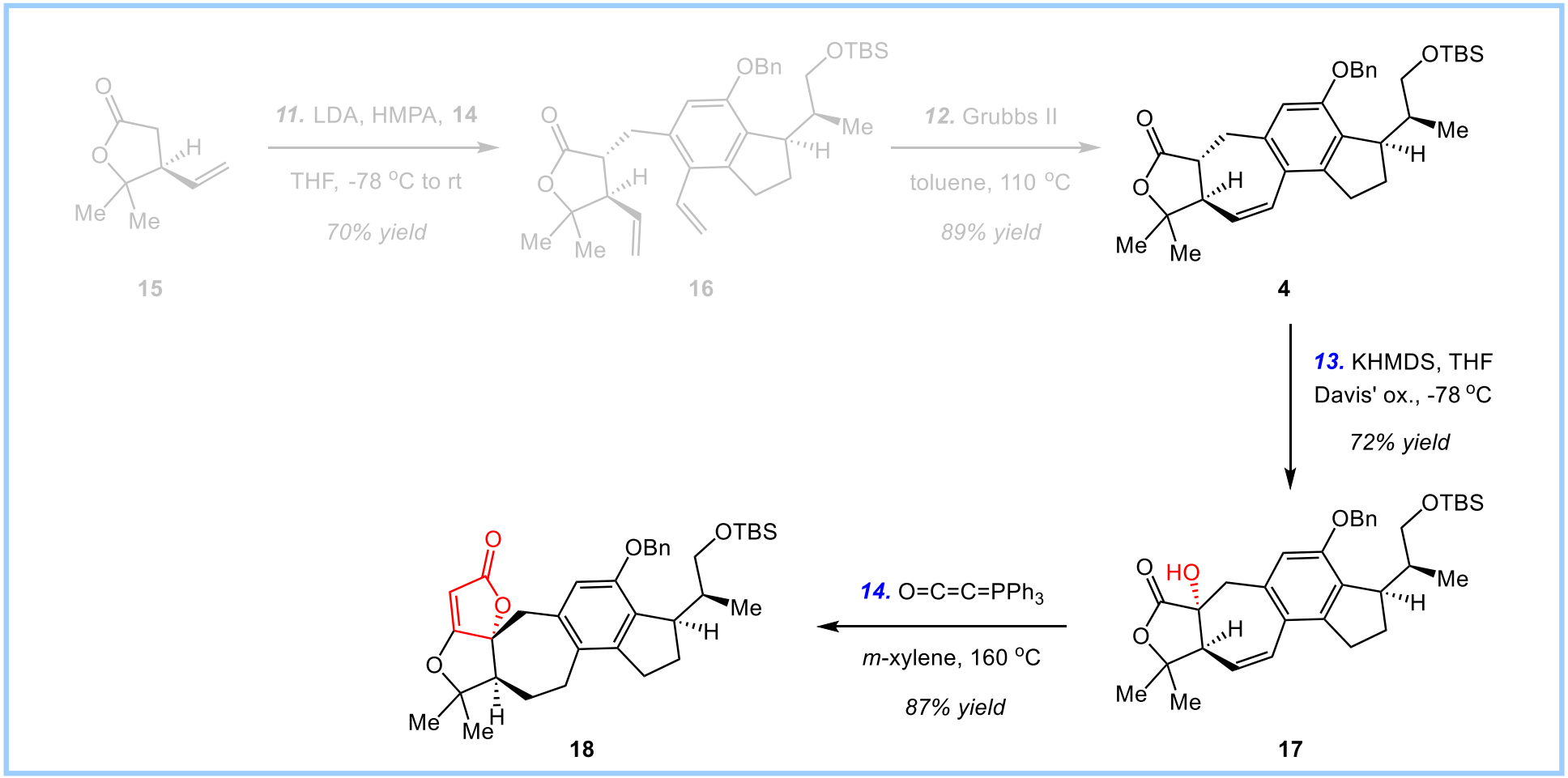
Synthesis of Compound 18



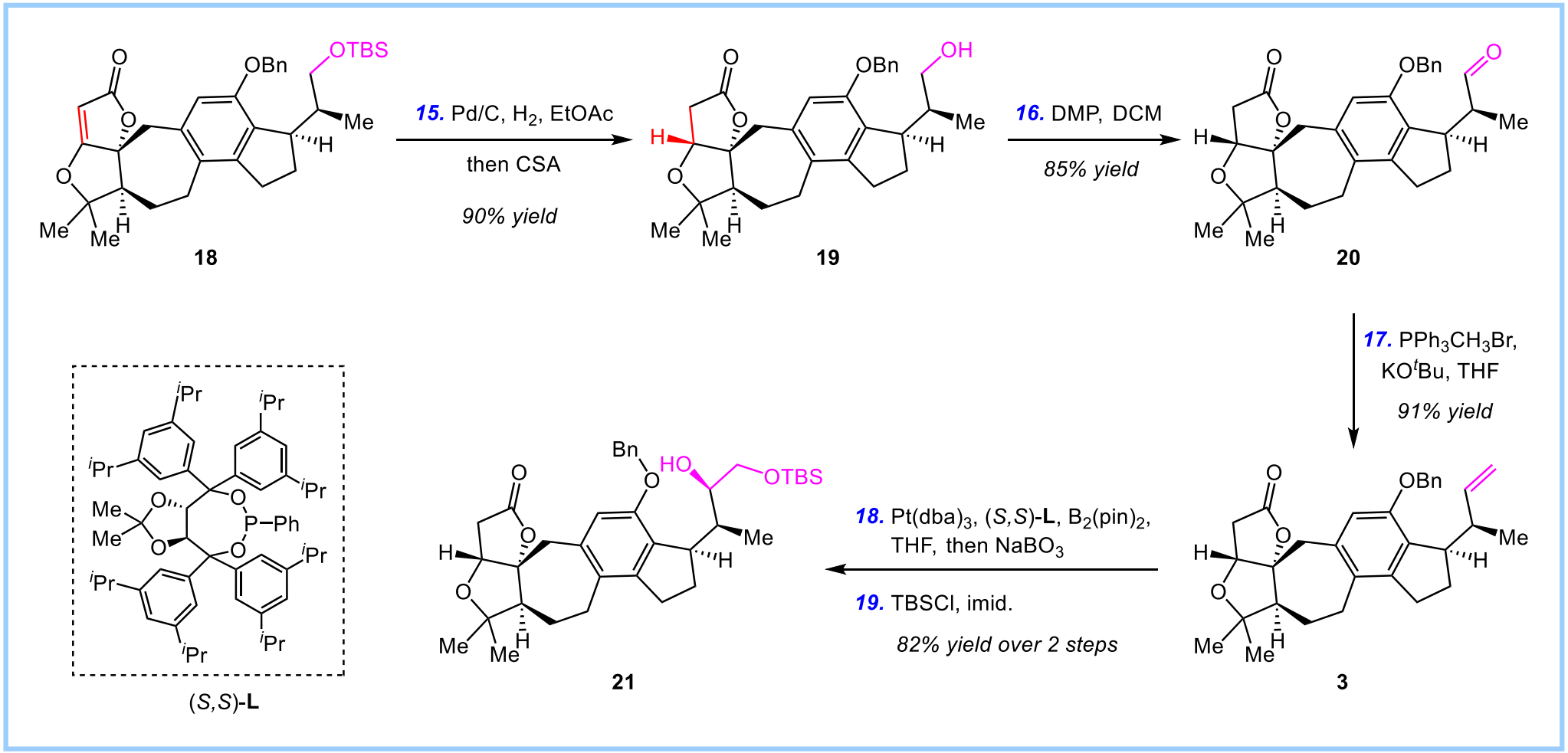
Synthesis of Compound 18



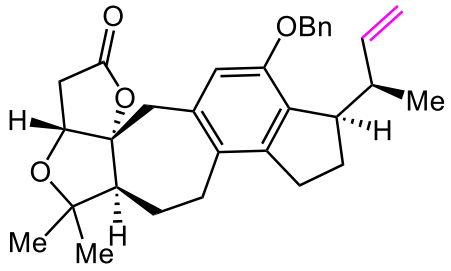
Synthesis of Compound 18



Synthesis of Compound 21



Synthesis of Compound 21

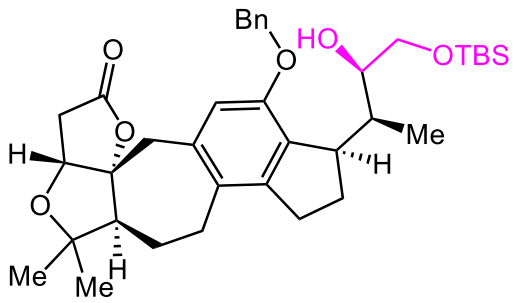


3

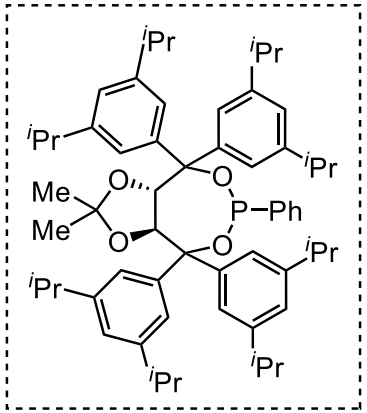
18. $Pt(dba)_3$, (*S,S*)-**L**, $B_2(pin)_2$, THF, then $NaBO_3$

19. TBSCl, imid.

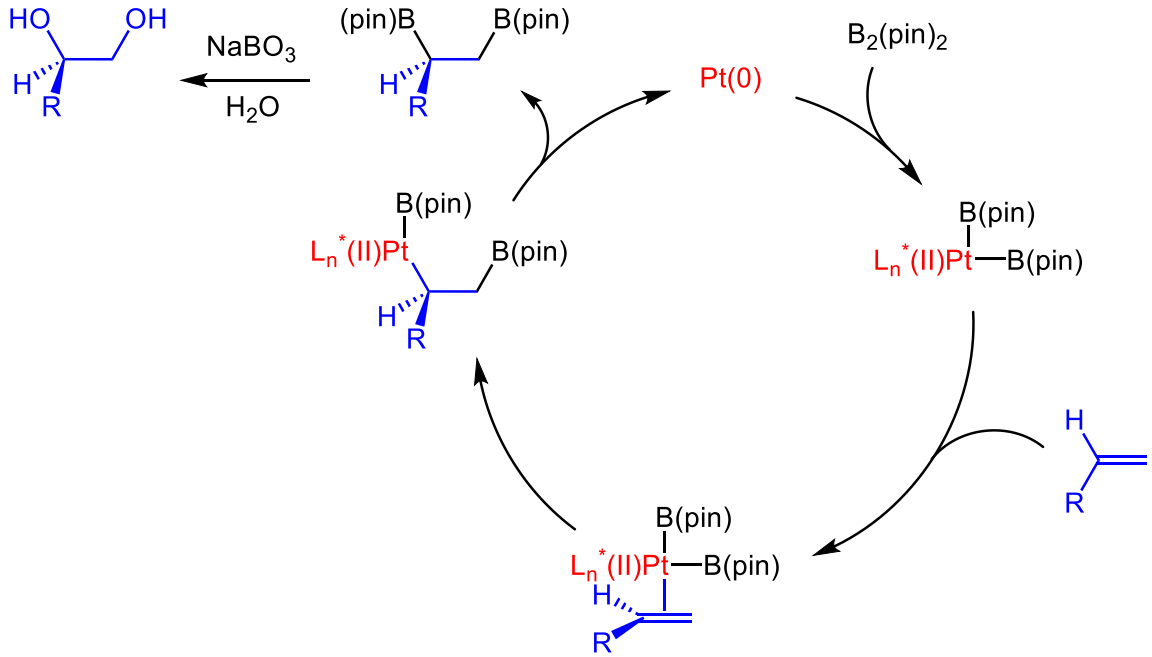
82% yield over 2 steps



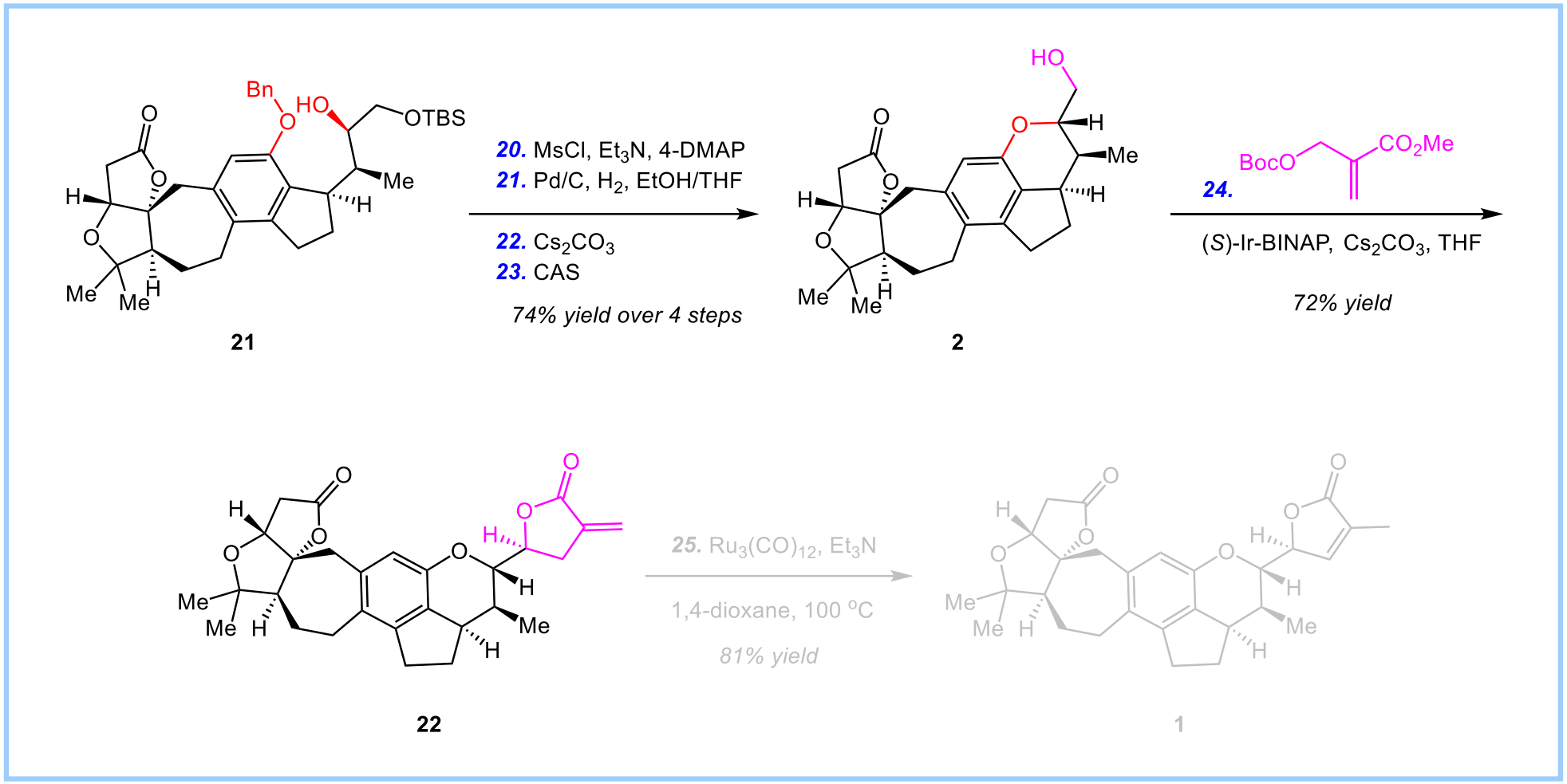
21



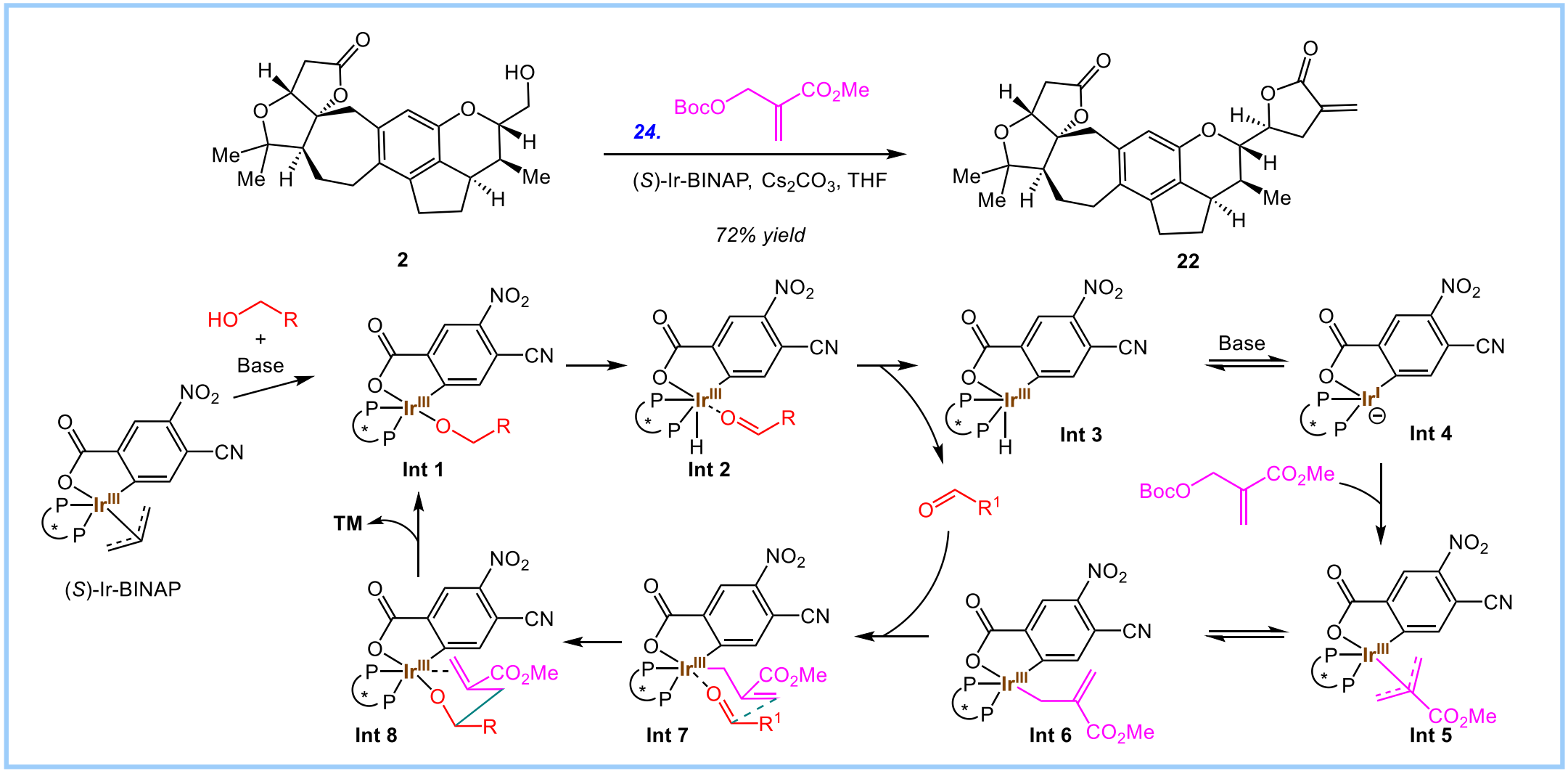
(*S,S*)-**L**



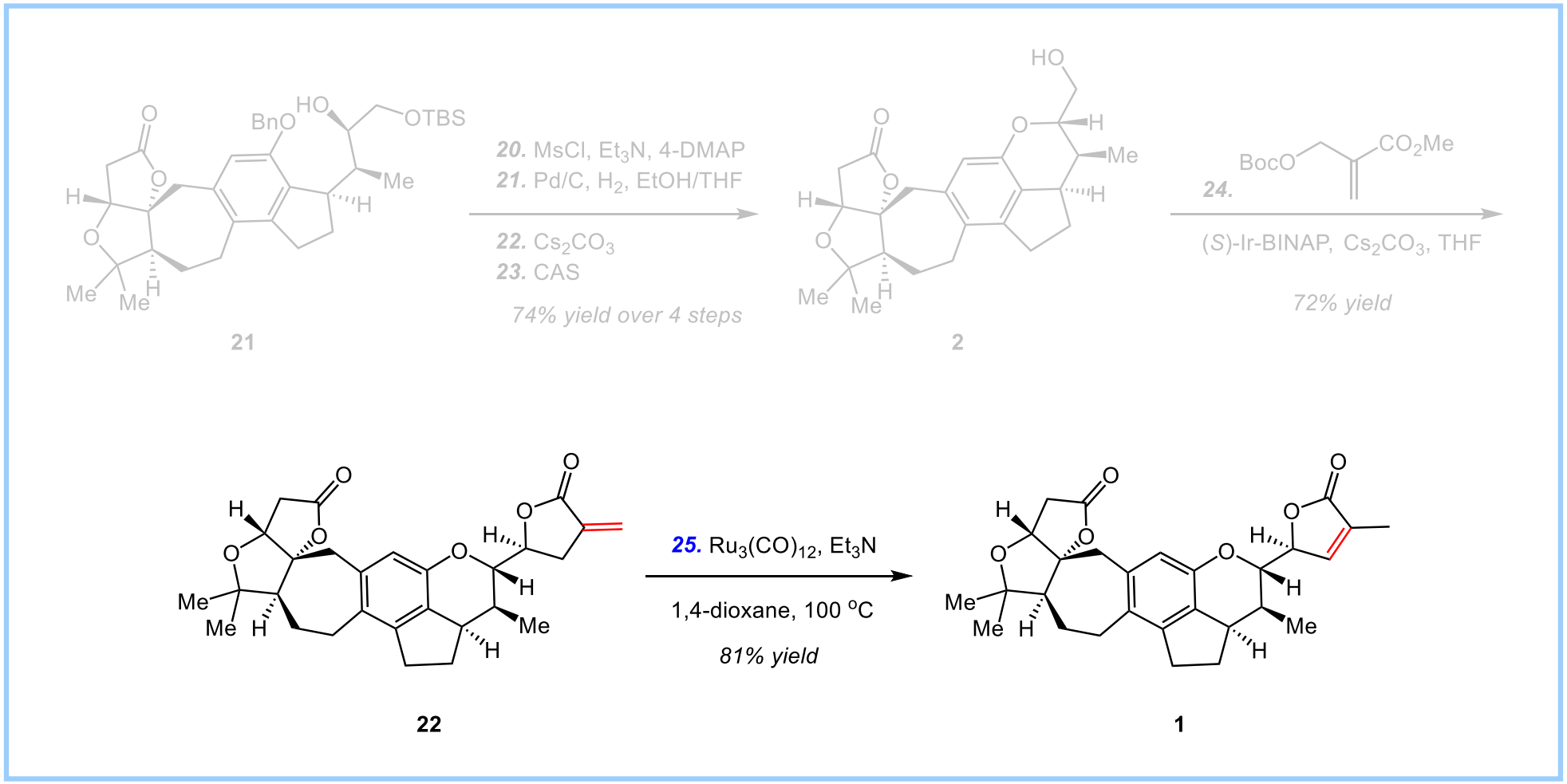
Synthesis of Compound 1



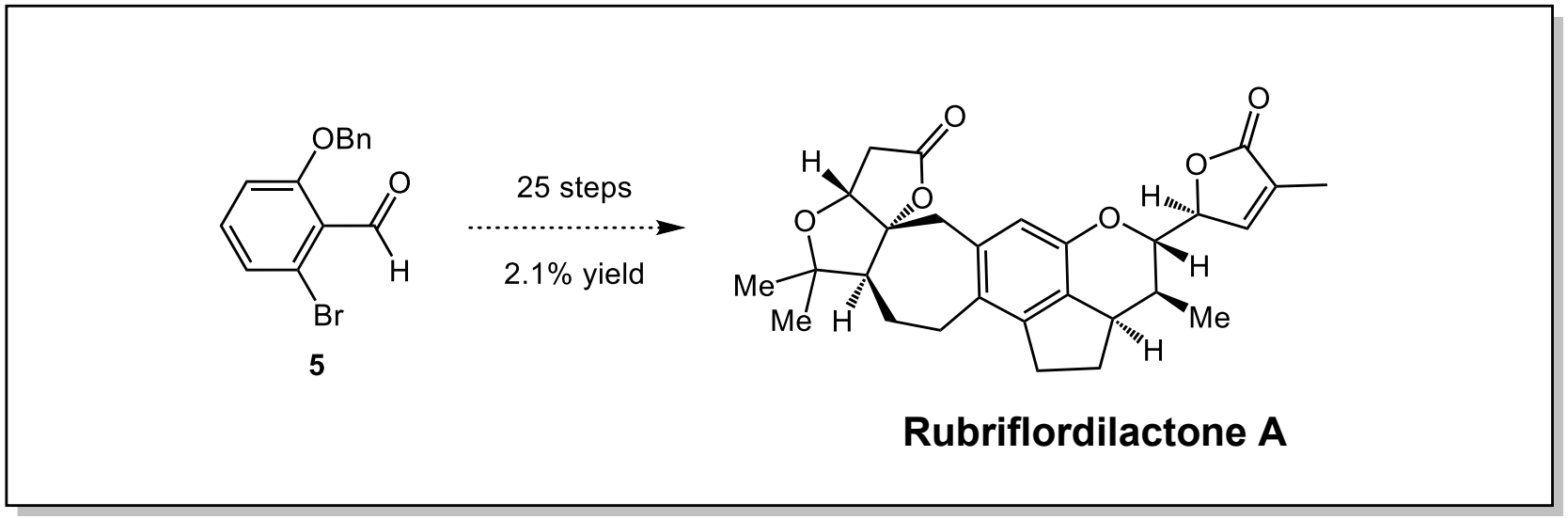
Synthesis of Compound 1



Synthesis of Compound 1



Summary



- Carreira's Ir/amine dual-catalyzed allylation stitch together C-sp3 and C-sp3 units;
- Morken's Pt-catalyzed diboration/oxidation to adjust the chiral center;
- Krische's Ir-catalyzed reaction to access γ-butenolide stereospecifically.

Writing Strategy

First paragraph

Structure

↓

Origin and History

- Plants from the family Schisandraceae are recognized as rich sources of lignans with diverse biological activities. Over the past two decades, however, many novel, highly oxygenated nortriterpenoids have been isolated from Schisandra species, primarily by Sun and colleagues.
- The ongoing discovery of unprecedented natural products not only enriches the phytochemical exploration of terpenoids but also presents a legion of significant challenges for the synthetic community. In 2011, Z. Yang's group accomplished the first total synthesis of Schindilactone A , which was celebrated as a ground-breaking milestone in the laboratory chemical synthesis of such challenging terpenoids……

Writing Strategy

Last paragraph

Summary

↓

Committed Steps

↓

Prospect

- In conclusion, we have developed an enantioselective total synthesis of (+)-Rubriflordilactone A (**1**), a complicated heptacyclic Schisandra nortriterpenoid.
- A key feature of this synthesis is the late-stage use of Krische's Ir-catalyzed 2-(alkoxycarbonyl)allylation of unprecedently complex alcohol **4** to form γ-butenolide stereospecifically. To the best of our knowledge, it represents the first example of this reaction strategically applied to the natural product synthesis……
- Finally, the superb stereocontrol of multiple contiguous stereogenic centers associated with the right domain, particularly utilizing the stereodivergence of Ir/amine catalysis, allows this strategy to be extended naturally to the unified synthesis of rubriflordilactone B (2), which will be reported in due course.

Representative Examples

- These two distinct ring formation strategies were again employed in their subsequent syntheses of rubriflordilactone B (**2**) and pseudorubriflordilactone B (**3**), respectively. (*adj*. 不同的，明显的)

- As anticipated, Krische's Ir-catalyzed 2-(alkoxycarbonyl)allylation proved effective in our highly intricate substrate **4**. (预见，预料(并做准备)，期望，盼望)

- Drawing inspiration from our recent work on the synthesis of Stemona alkaloids and considering the mild conditions used, as well as the excellent stereoselectivity of the Krische catalyst, we anticipated that strict stereocontrol over C23 would be readily accessible, even with a highly complex substrate like **4**.(从…中获得灵感)

Acknowledgment

Thanks for your attention!