ASAP

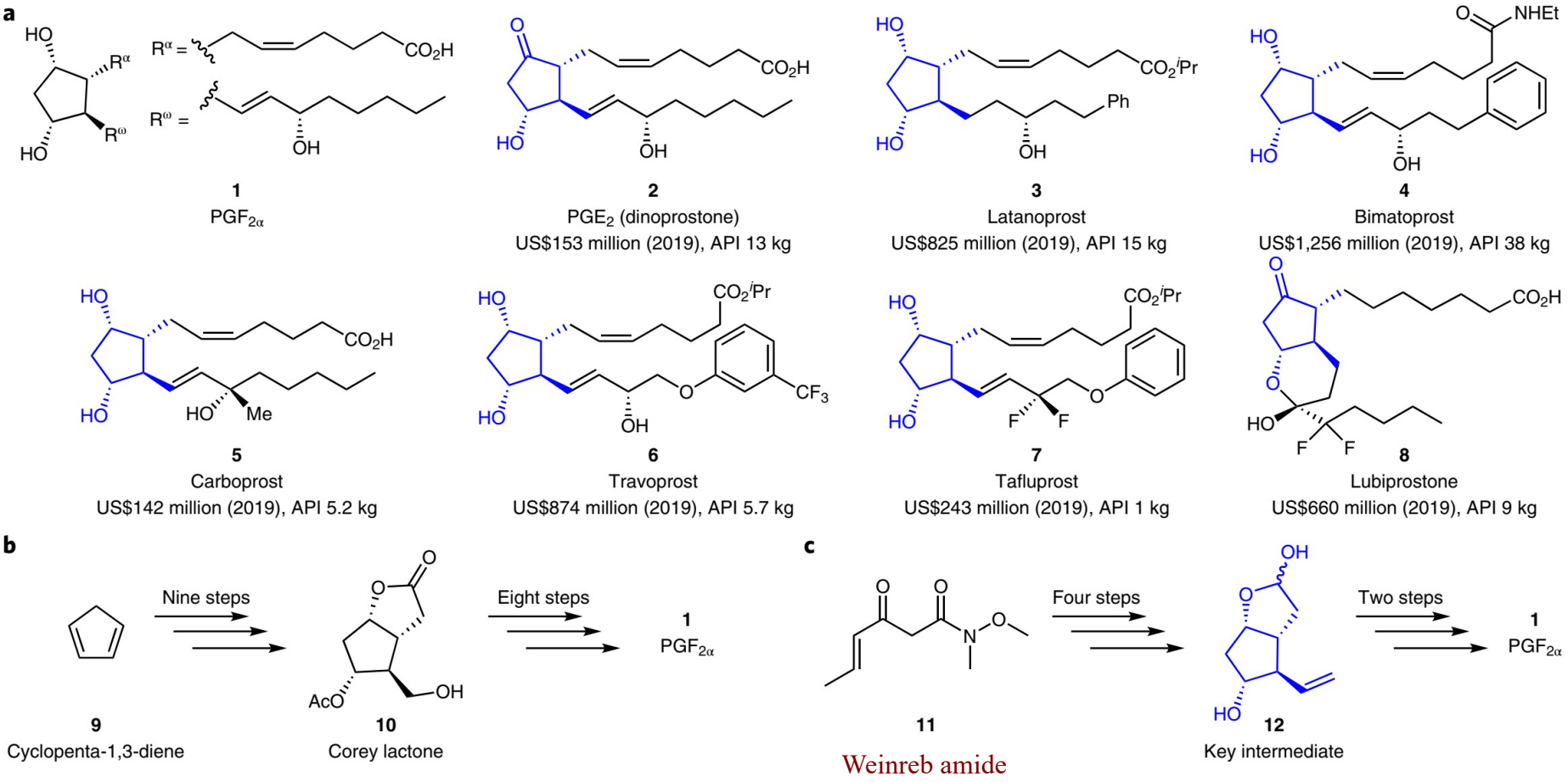
Reporters: Yi Xiao

Supervisors: *Prof*. Tao Ye

***Dr*. Yian Guo**

June 28st, 2021

Part I: Concise, Scalable and Enantioselective Total Synthesis of Prostaglandins



Zhang, F., Zeng, J., Gao, M. et al. Nat. Chem. (2021). https://doi.org/10.1038/s41557-021-00706-1

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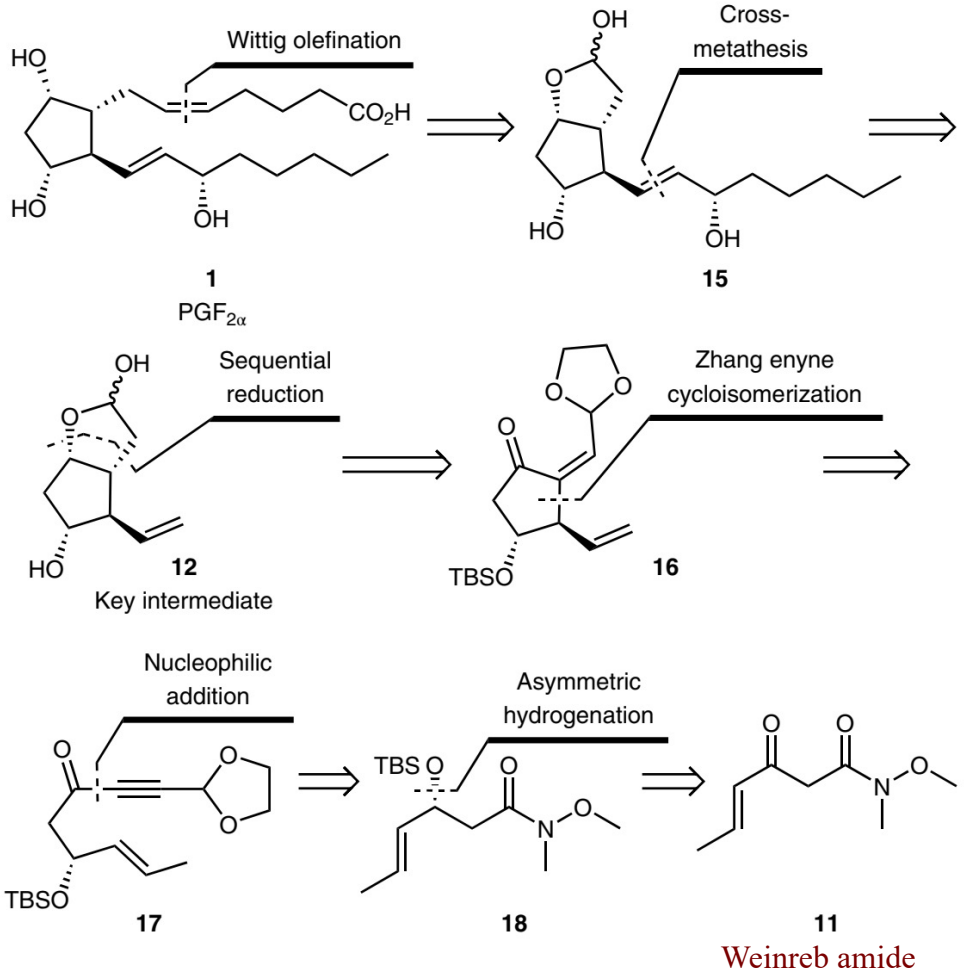

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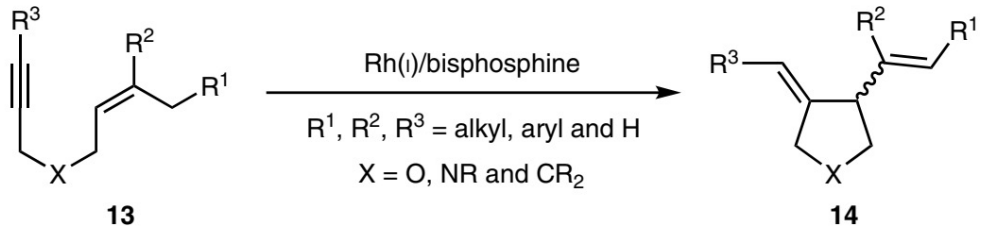

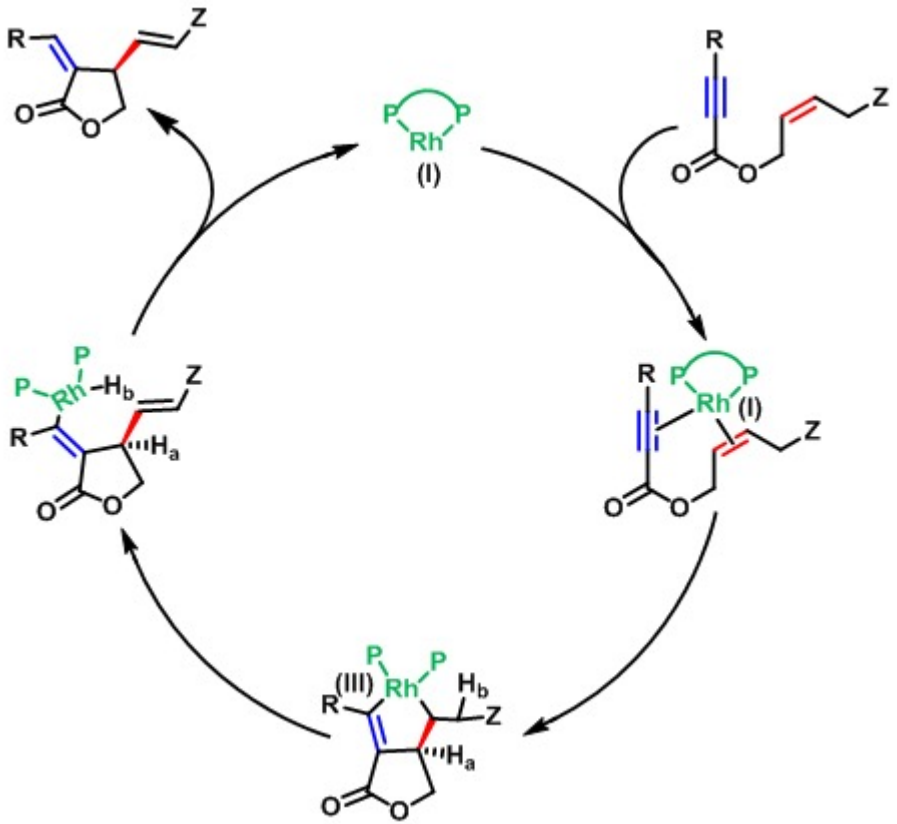

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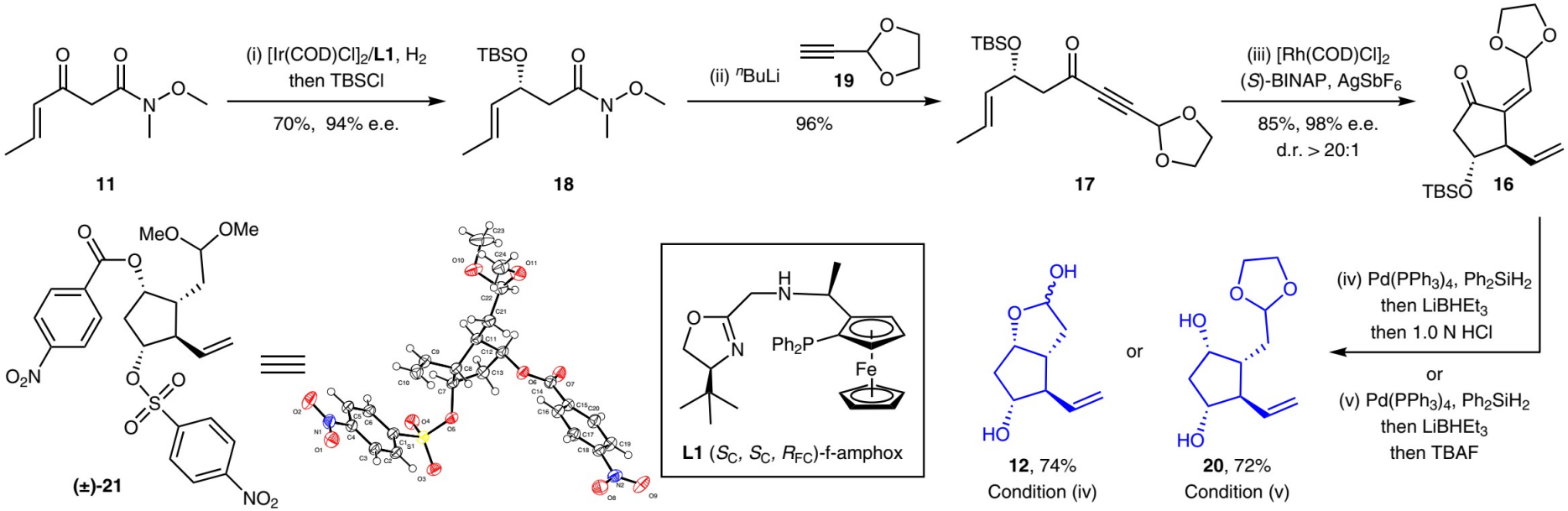
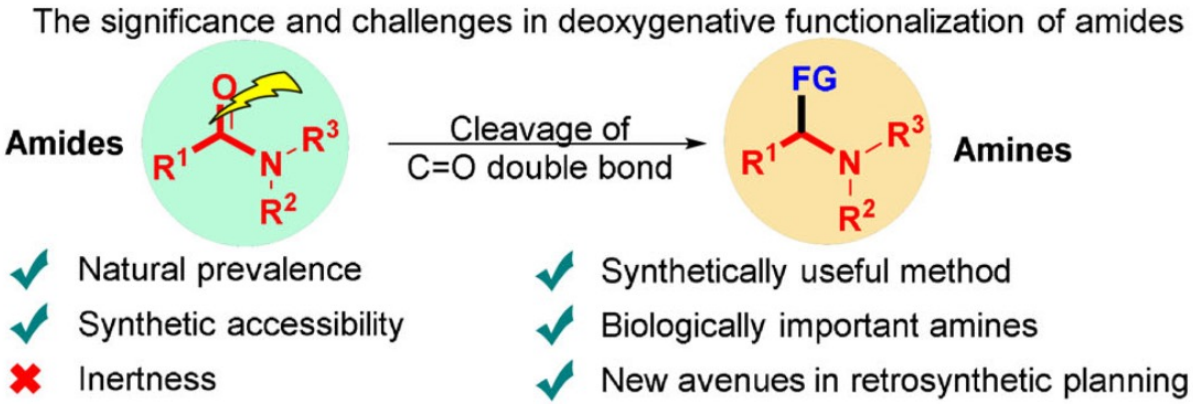
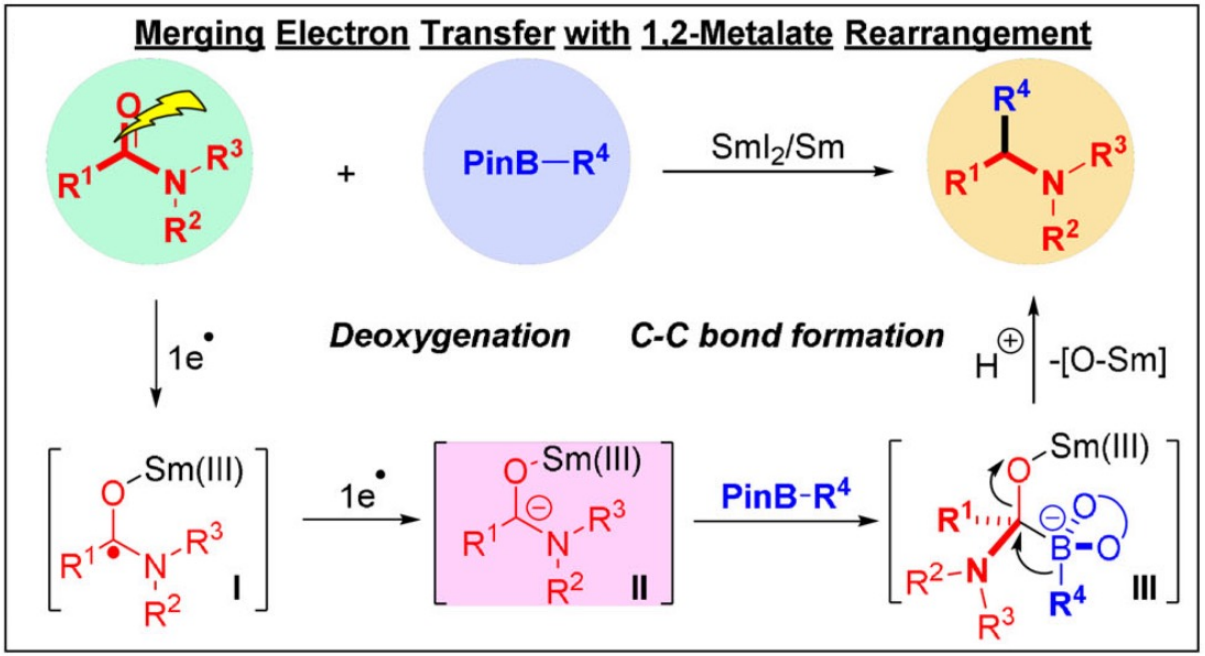


Zhang, F., Zeng, J., Gao, M. et al. Nat. Chem. (2021). https://doi.org/10.1038/s41557-021-00706-1

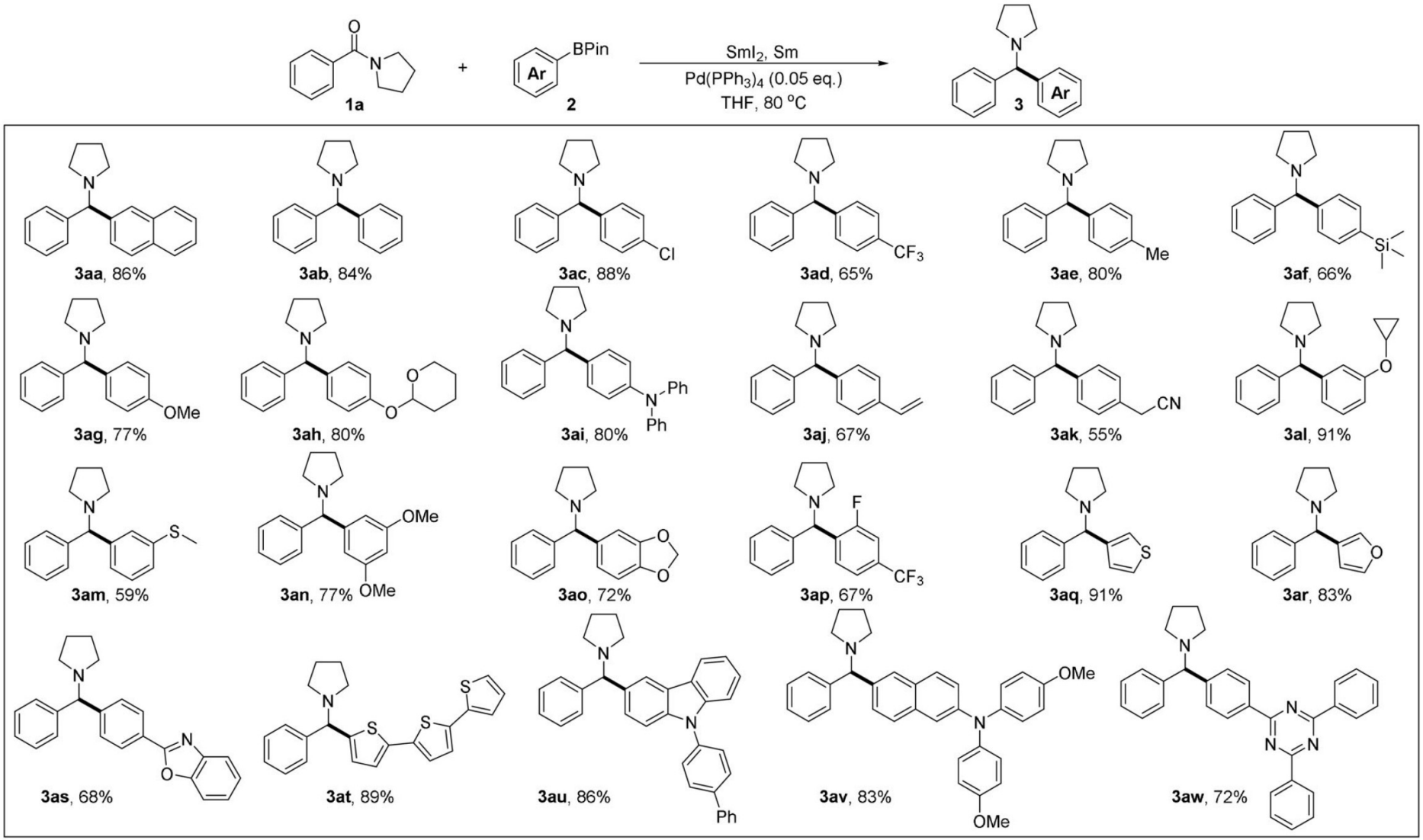
Part II: Merging Electron Transfer with 1,2-Metalate Rearrangement: Deoxygenative Arylation of Aromatic Amides with Arylboronic Esters





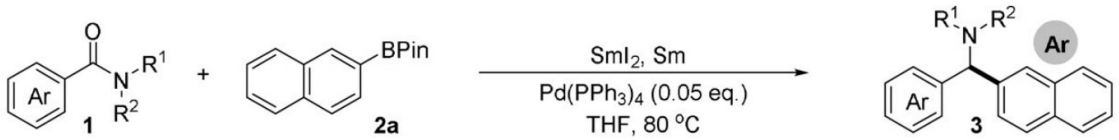
X. M. Wang., *Angew. Chem. Int. Ed*. **2021**, *60*, 2-8.

Part II: The scope of aryl boron reagents

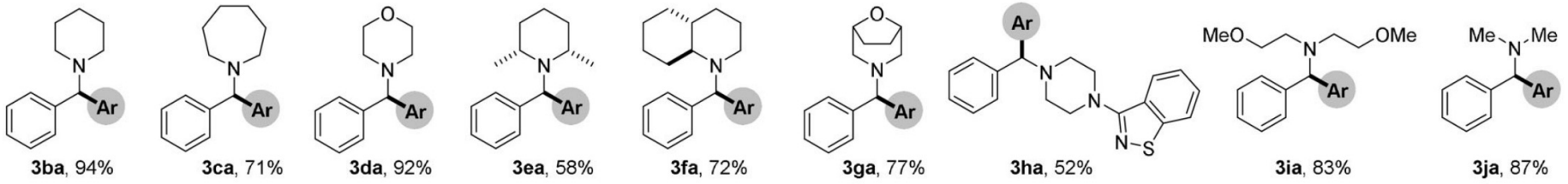


X. M. Wang., *Angew. Chem. Int. Ed*. **2021**, *60*, 2-8.

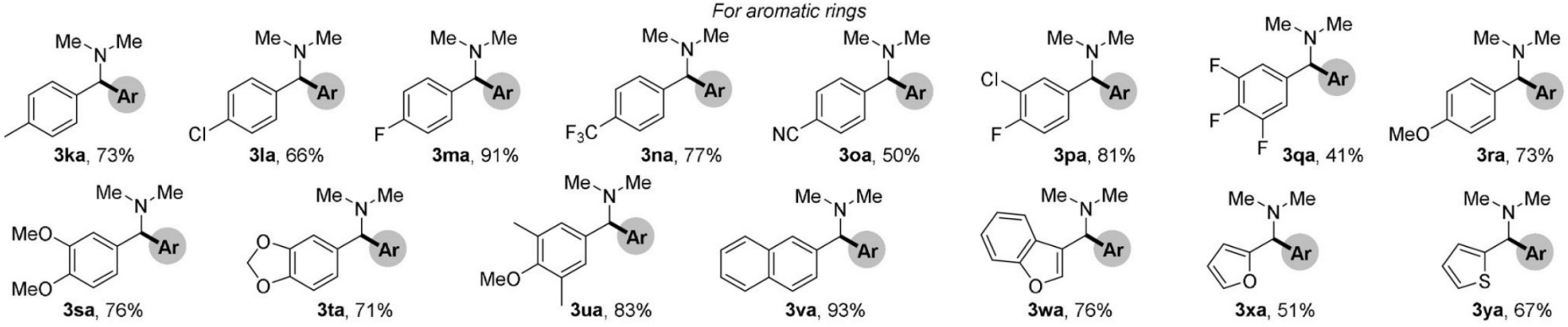
Part II: The scope of aryl amides



For substituent groups of N atom

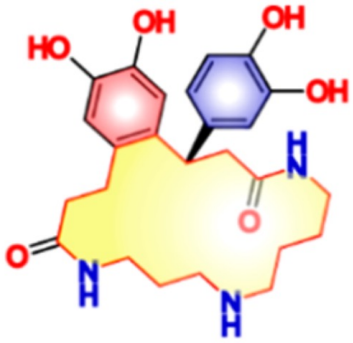


For aromatic rings

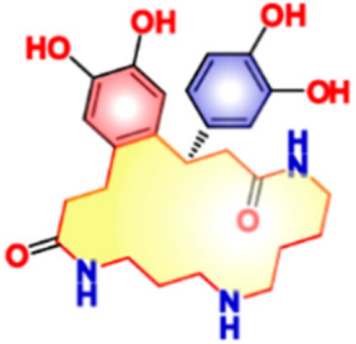


X. M. Wang., *Angew. Chem. Int. Ed*. **2021**, *60*, 2-8.

Part III: Designing Retrosynthesis of Scocycamides



(+)-(S)-scocycamide



(-)-(S)-scocycamide

Isolation

- They were isolated from the roots of *Scopolia tangutica.*

Features

- They featured a unique 6/18 fused bicyclic framework with spermidine and catechol units, representing a new subtype of natural spermidine alkaloids.

Biological activities:

- They inhibited butyrylcholinesterase and exhibited antioxidant capacity, suggesting beneficial constituents against Alzheimer's disease and oxidation.

Org. Lett. **2020**, *22*, 8240-8244

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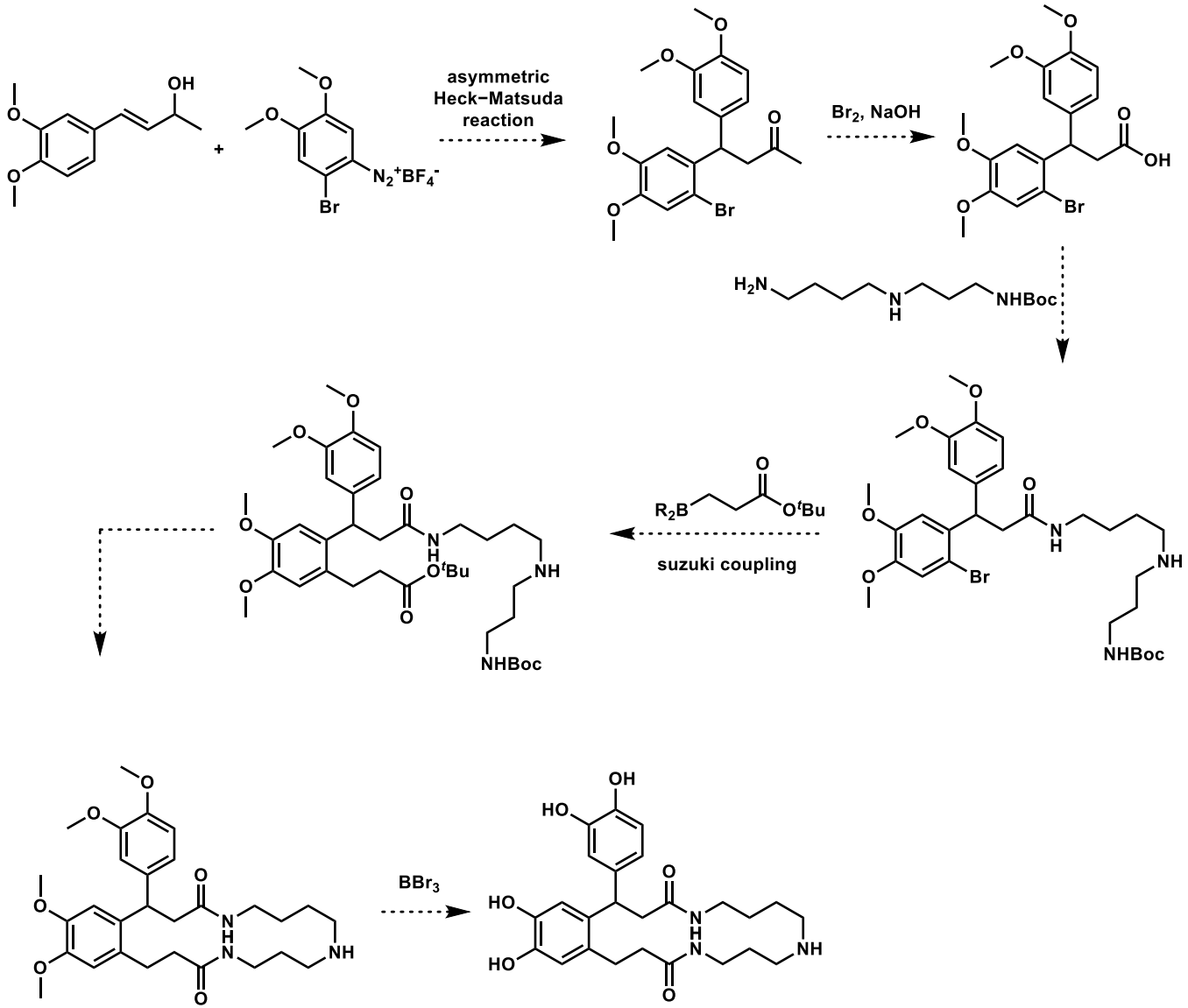
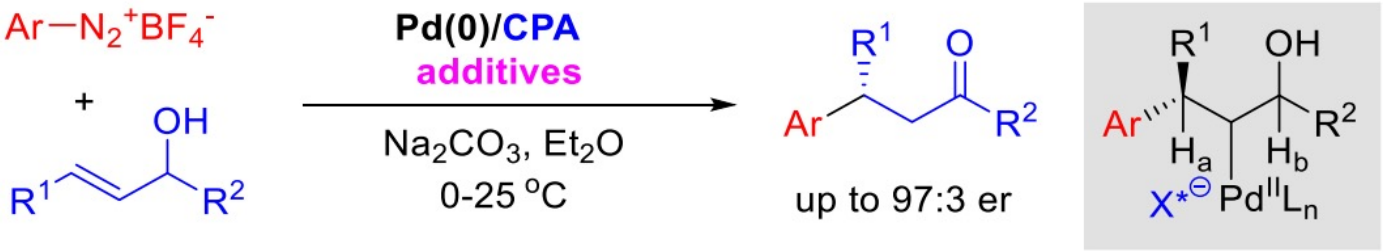
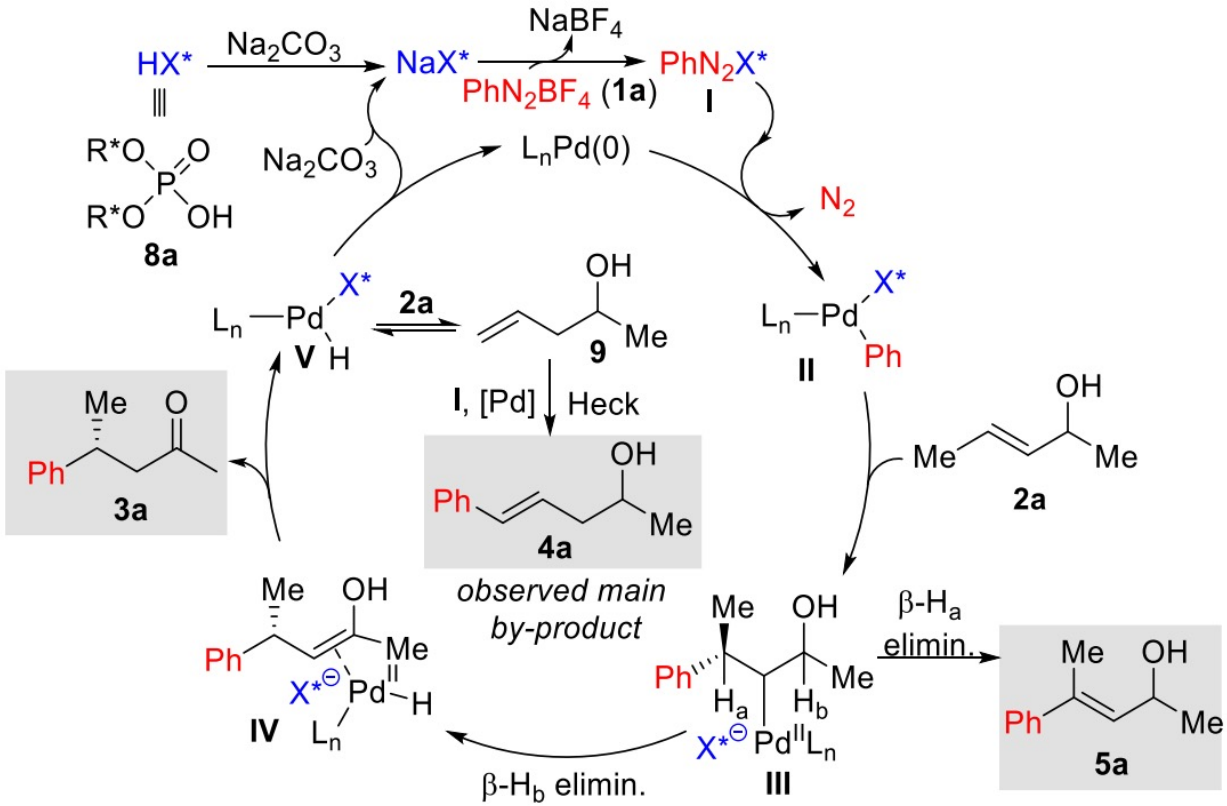


Part III: Chiral Anion-Mediated Asymmetric Heck-Matsuda Reaction of Acyclic Alkenyl Alcohols





Org. Lett. **2020**, *23,* 1473-1477

Author

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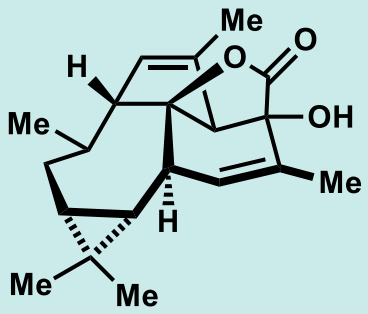
Experiences

1984, University of Illinois at Urbana-Champaign, B.S. Scott E. Denmark;
1990, Harvard University, Ph.D. David A. Evans;
1992, California Institute of Technology, Postdoctoral, Peter Dervan;
1996, California Institute of Technology, Assistant Professor;
1997, California Institute of Technology, Professor;
1998-present, Swiss Federal Institute of Technology Zurich, Professor.
2021-present, the Editor-in-Chief of JACS

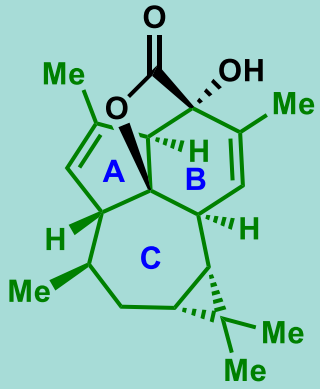
Research interests

Natural products total synthesis, catalytic methods, chemical biology.

Background



(+)-Euphorikanin A (1)



5/6/7/3-fused skeleton

Isolation

- In 2016 by Zhang and co-workers and identified as a novel diterpenoid from the roots of *Euphorbia kansui*, commonly referred to as kansui.

Biological activities:

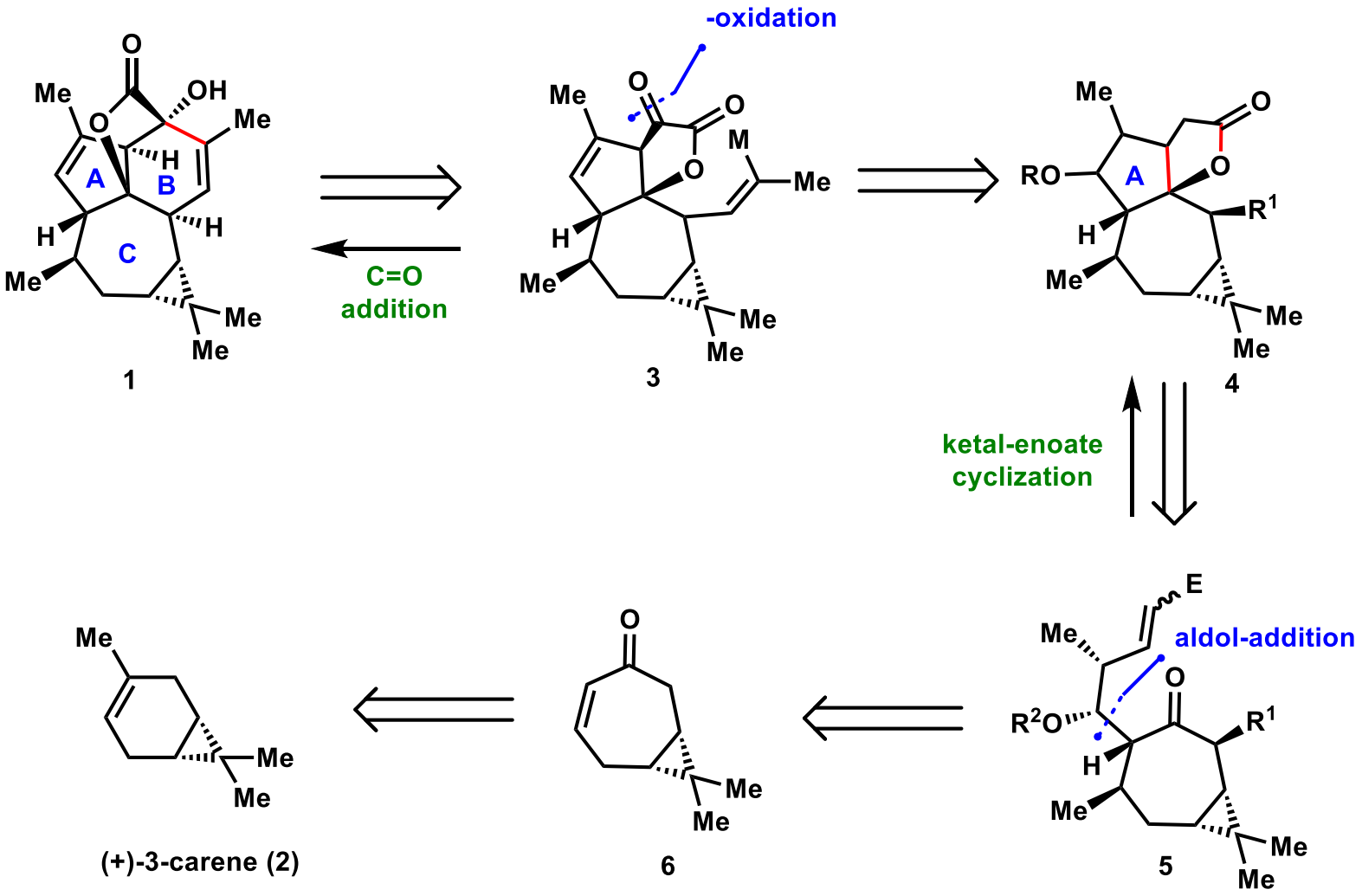
- It exhibited cytotoxicity against two human tumor cell lines (NCI-446 and HeLa).
- Extracts of the root have been widely used in traditional Chinese medicine, and they have been shown to reactivate latent HIV, potentially offering new therapeutic approaches for treatment of the disease.

Structural features

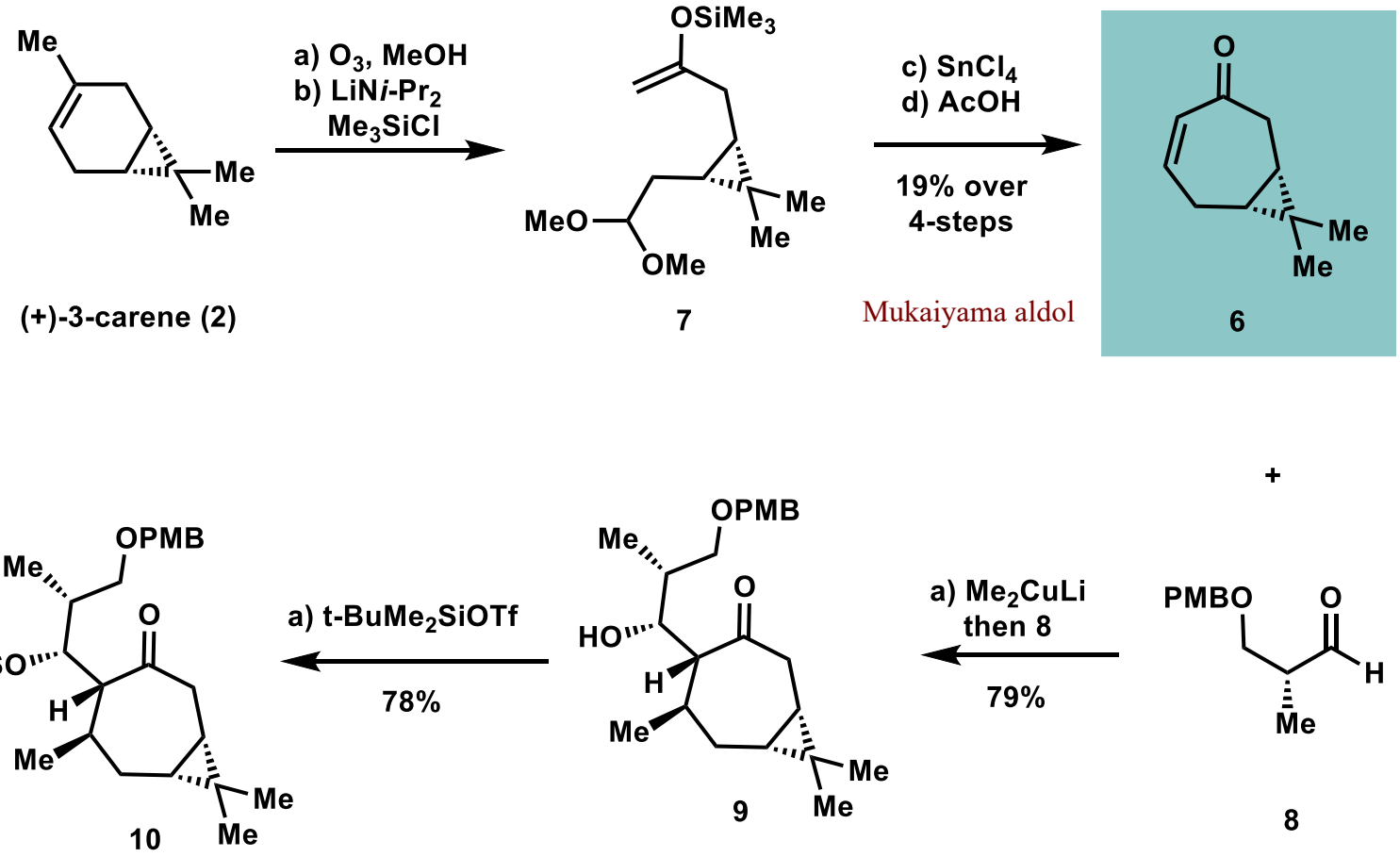
- Diterpenoid features a 5/6/7/3-fused tetracyclic skeleton, which harbors eight contiguous stereocenters.
- The structure includes a bridging [3.2.1]-γ-lactone substituted at the Cα-bridgehead with a hydroxy group.

Zhang, Z.-X., *Org. Lett*. **2016**, *18*, 2844-2847.

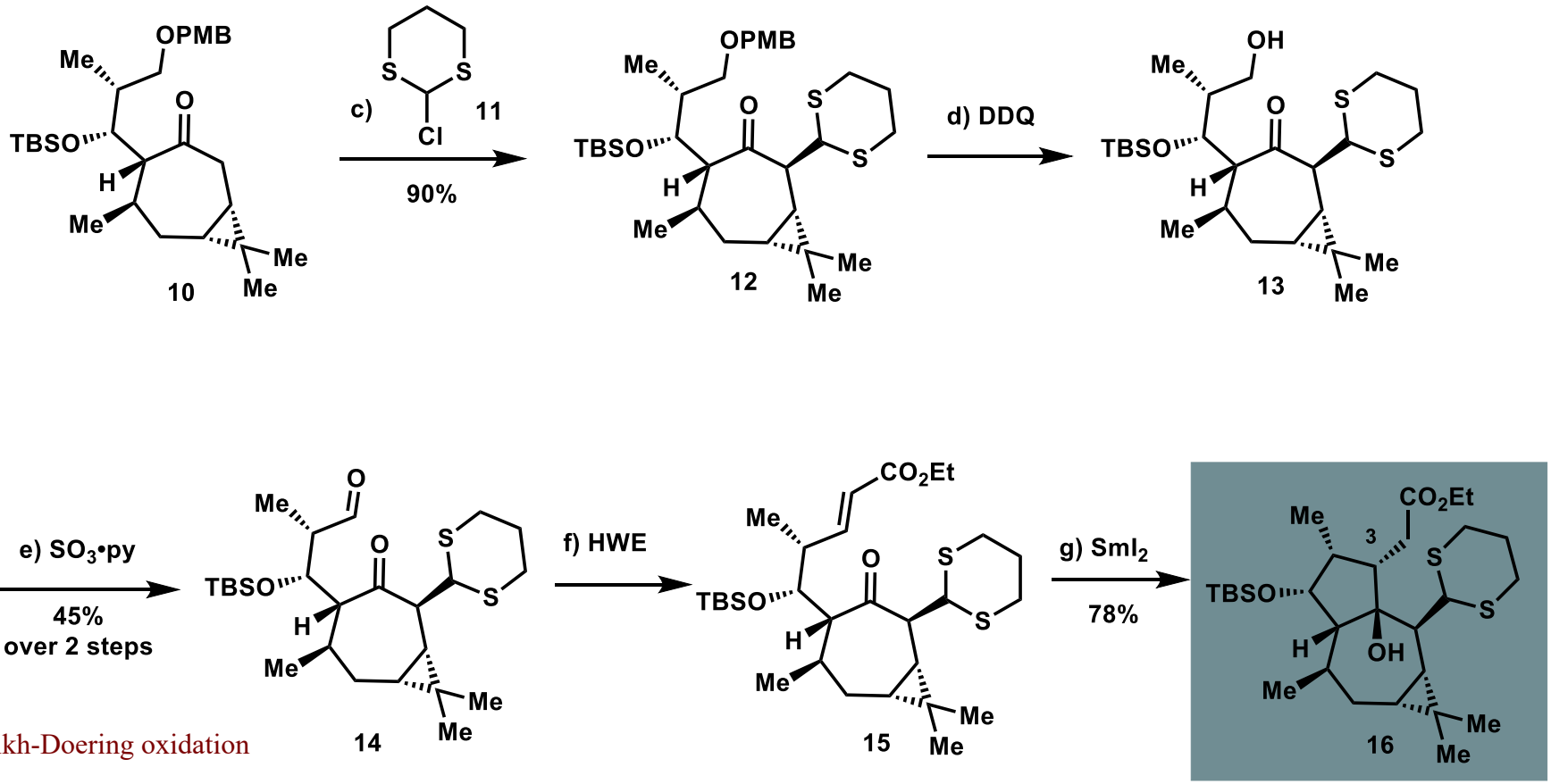
Retrosynthetic Analysis



Synthesis of Enone 6

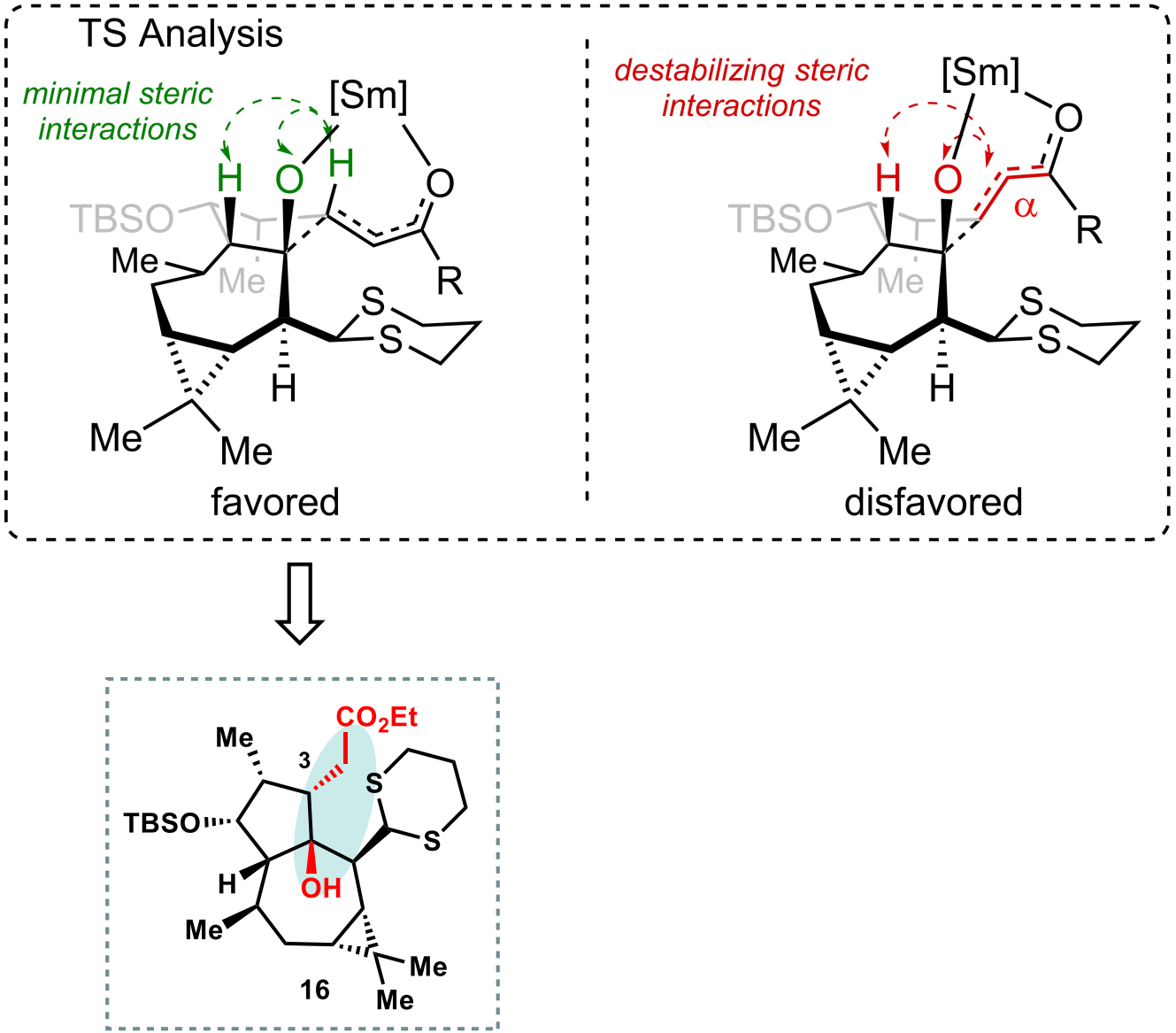


Initial Ketyl-Enoate Cyclization Attempt

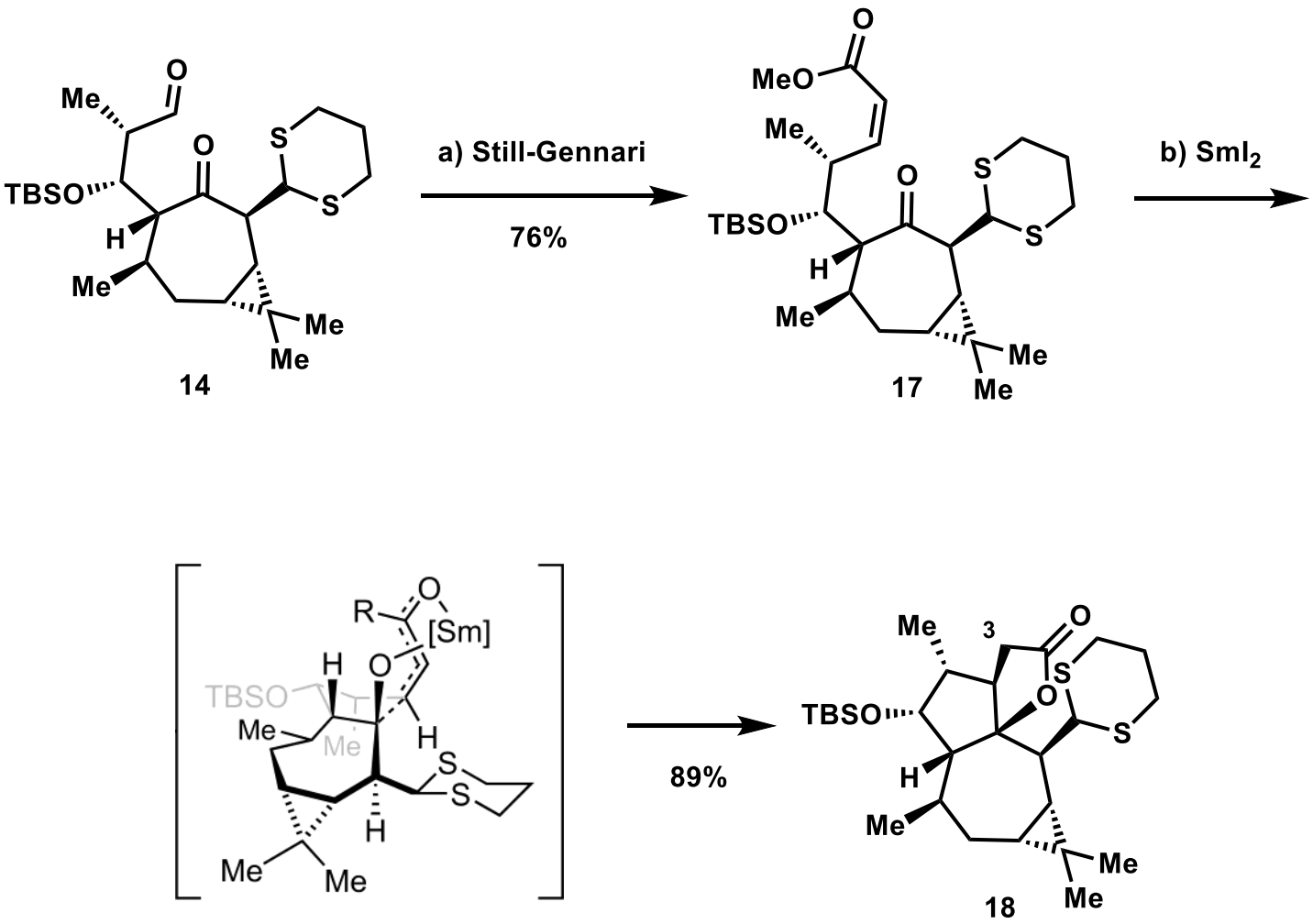


Parikh-Doering oxidation

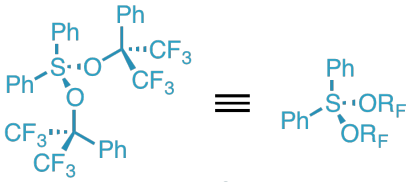
Transition State

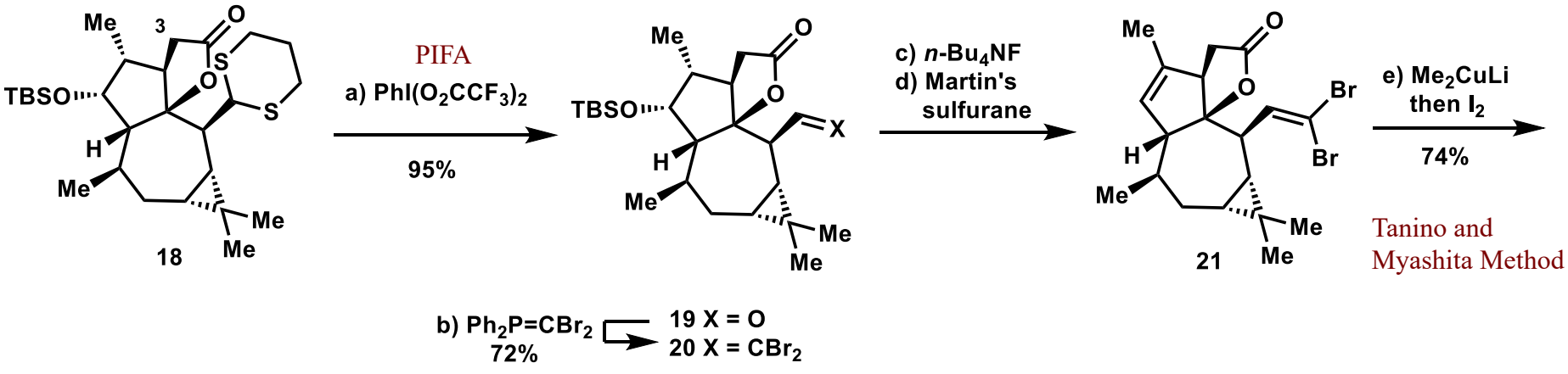


Synthesis of Lactone 18

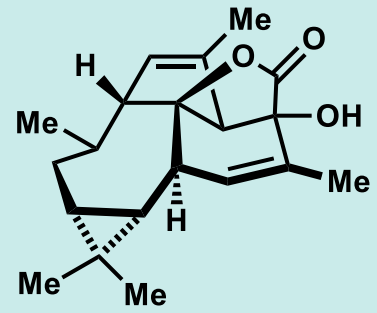


Completion of the Synthesis





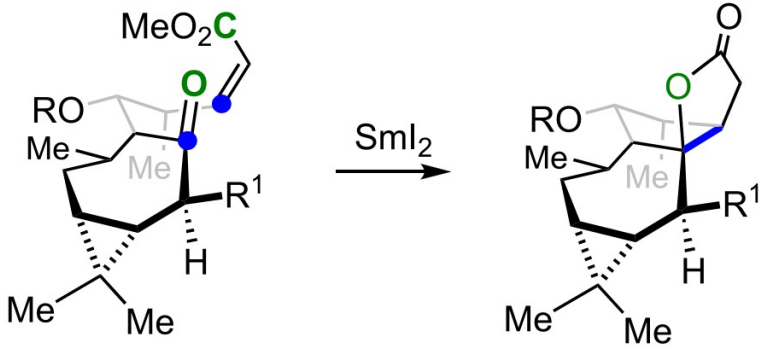
Summary



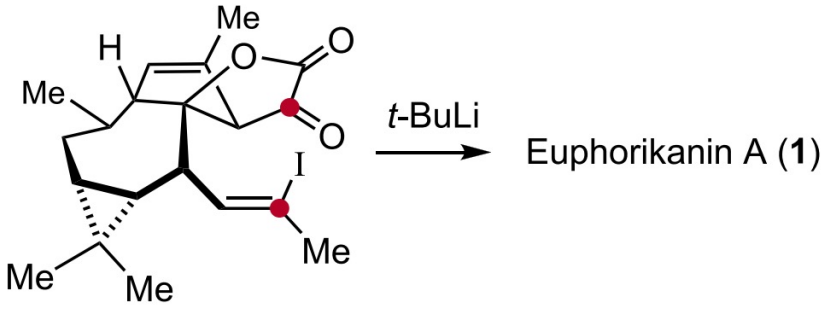
(+)-Euphorikanin A (1)

19 steps
first total synthesis

✓ *1-step Formation of A Ring & Lactone*

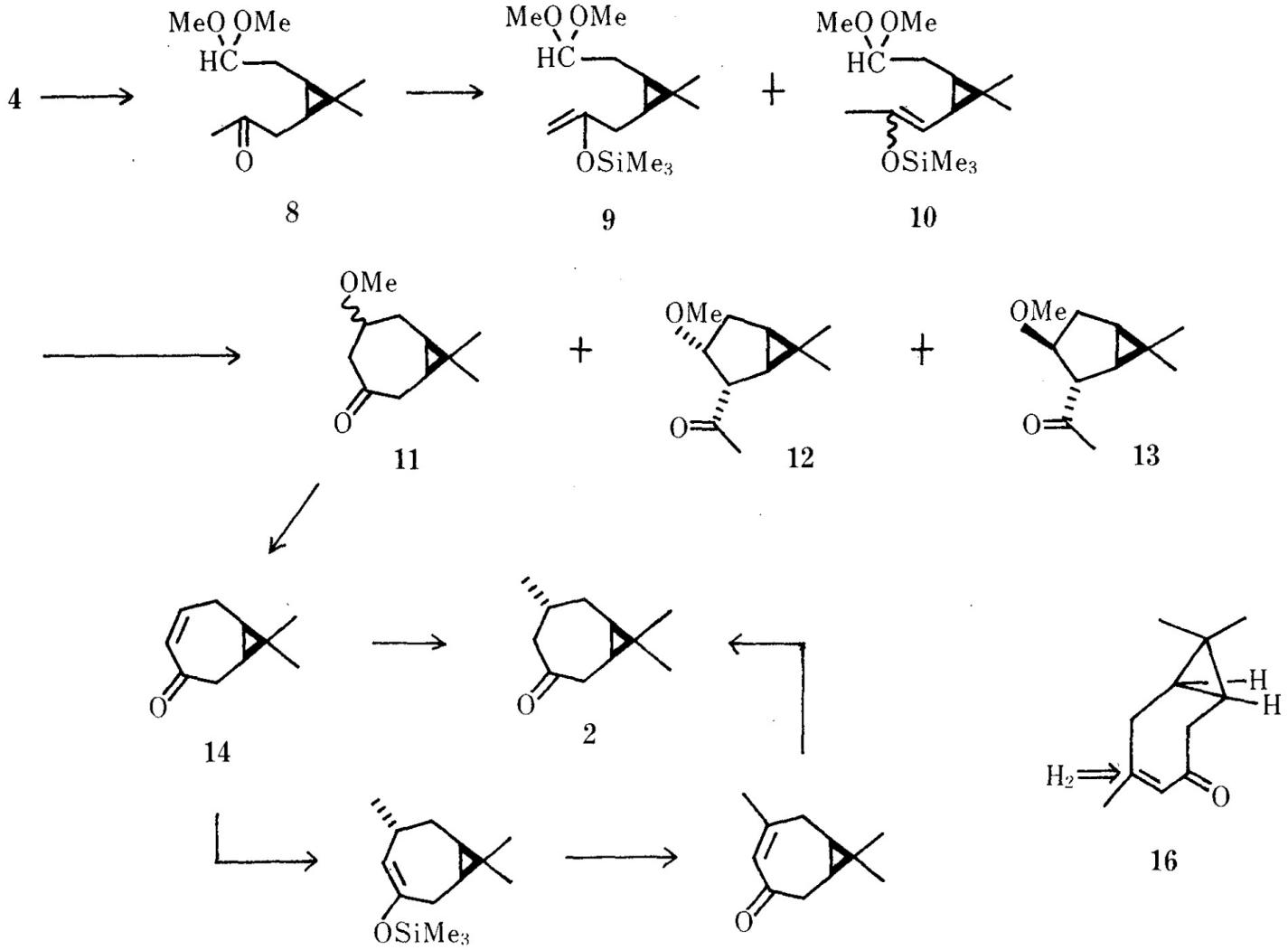


✓ *Metallation and Chemoselective Addition*

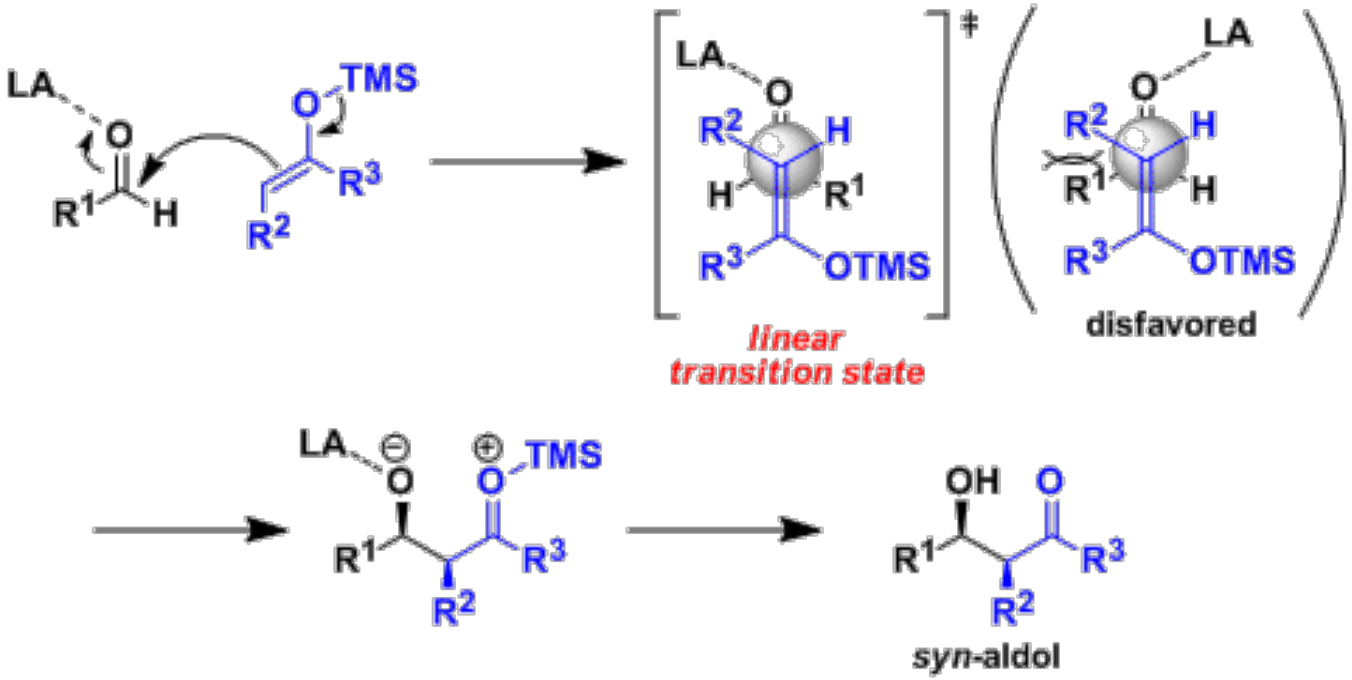


Synthesis of Enone 6

6

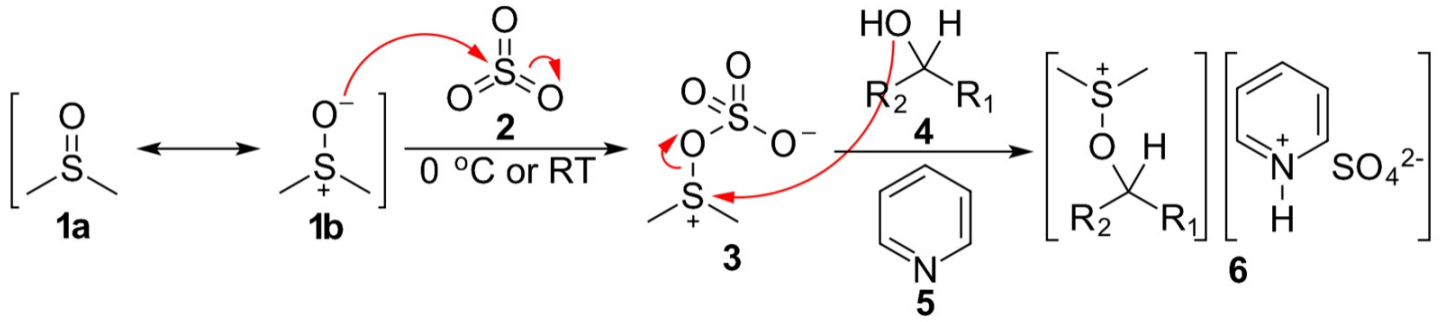

4
MeO OMe
HC
O
8
MeO OMe
HC
OSiMe3
9
MeO OMe
HC
OSiMe3
10
OMe
O
11
OMe
O
12
OMe
O
13
O
14
O
2
H
H
H2
O
16
OSiMe3
O

mukaiyama aldol reaction

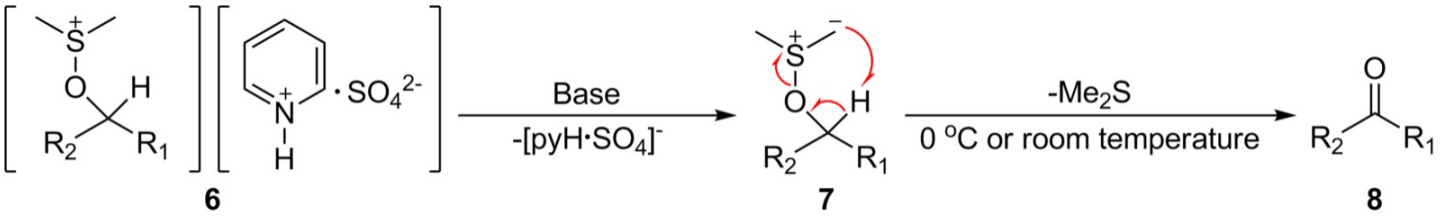


Parikh-Doering oxidation

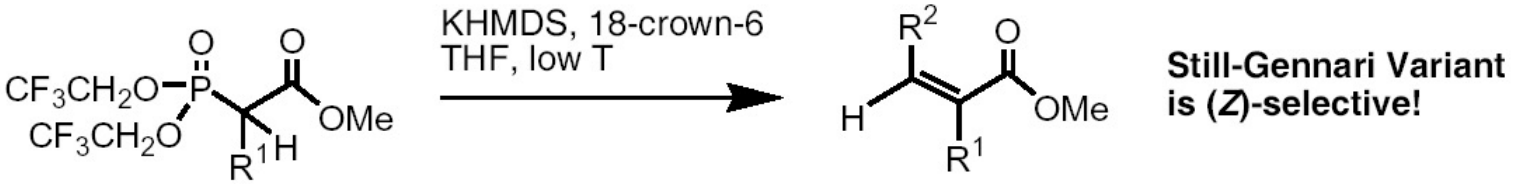
二甲亚砜与三氧化硫在0℃或室温下发生加成，并受到醇进攻，生成关键的烷氧基锍离子中间体(6)。



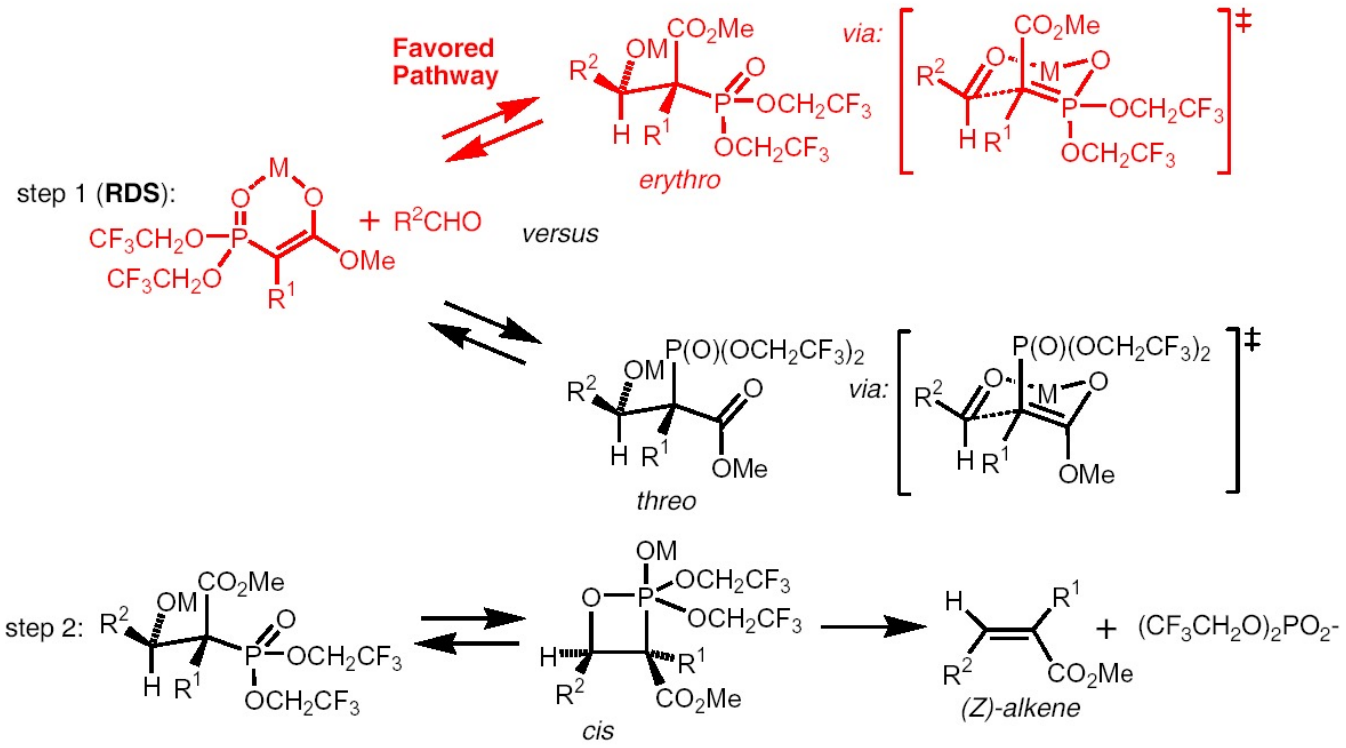
该中间体接下来被碱去质子化为相应的硫叶立德，然后硫叶立德经五元环过渡态、分解放出二甲硫醚，得到醛酮。



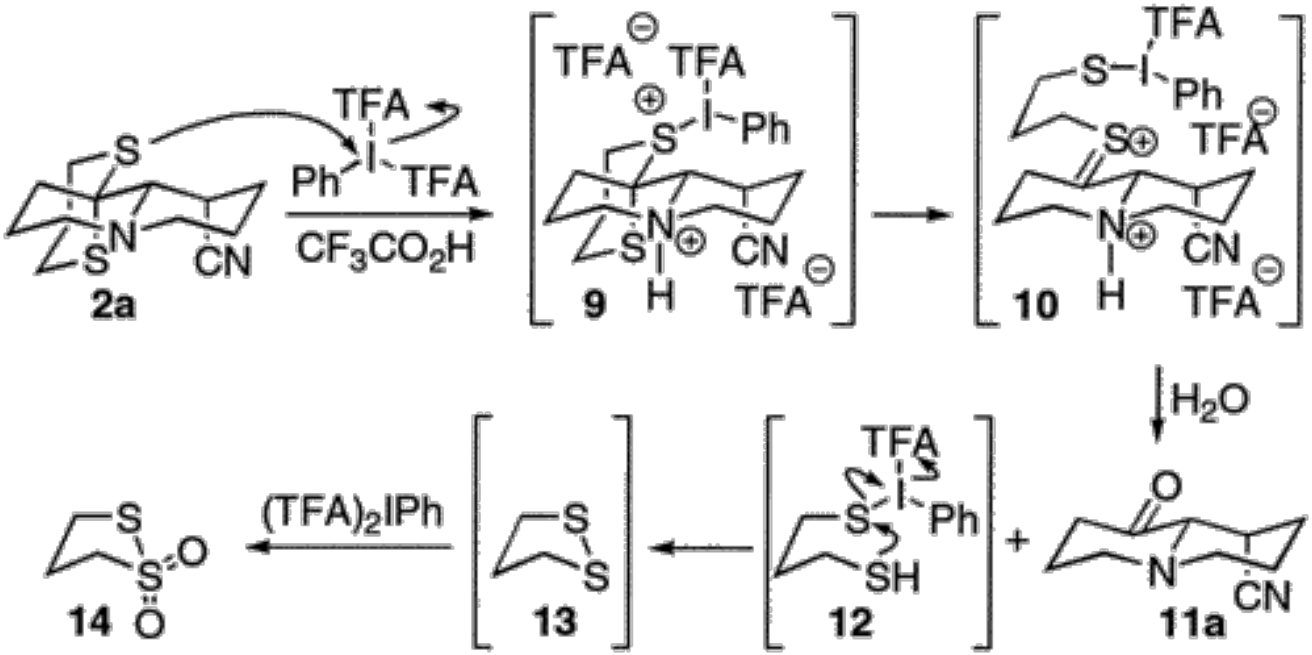
Still-Gernnari Reaction



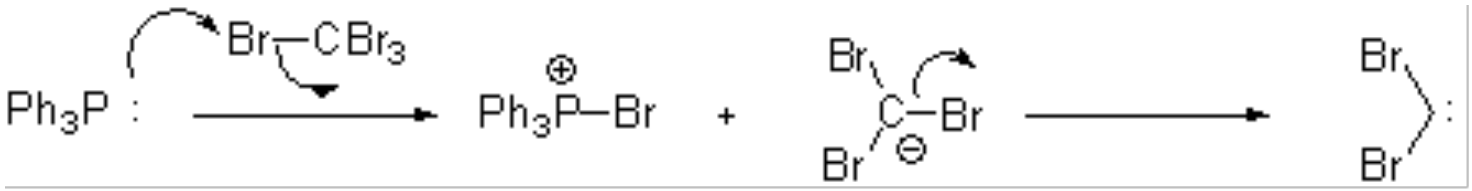
Mechanism Based Hypothesis:

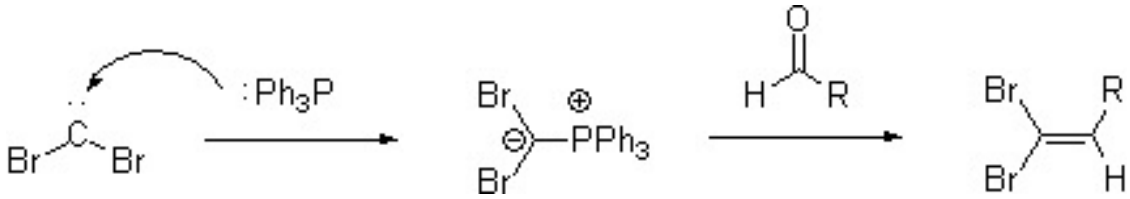


PIFA remove dithiane

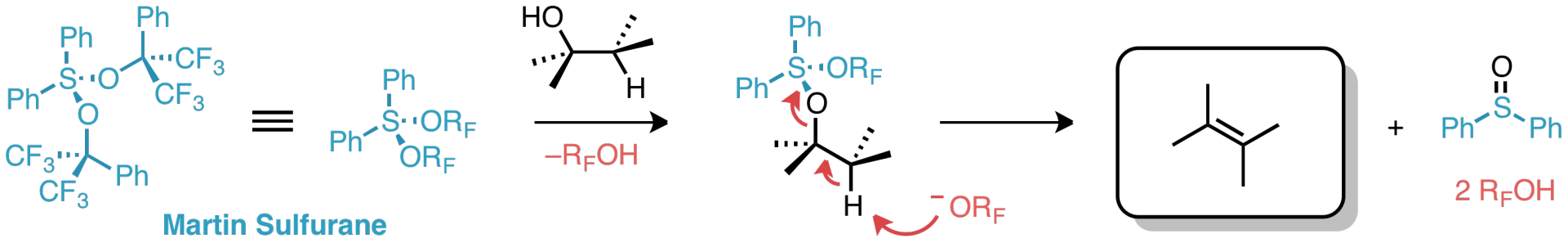


Ramirez–Corey–Fuchs reaction

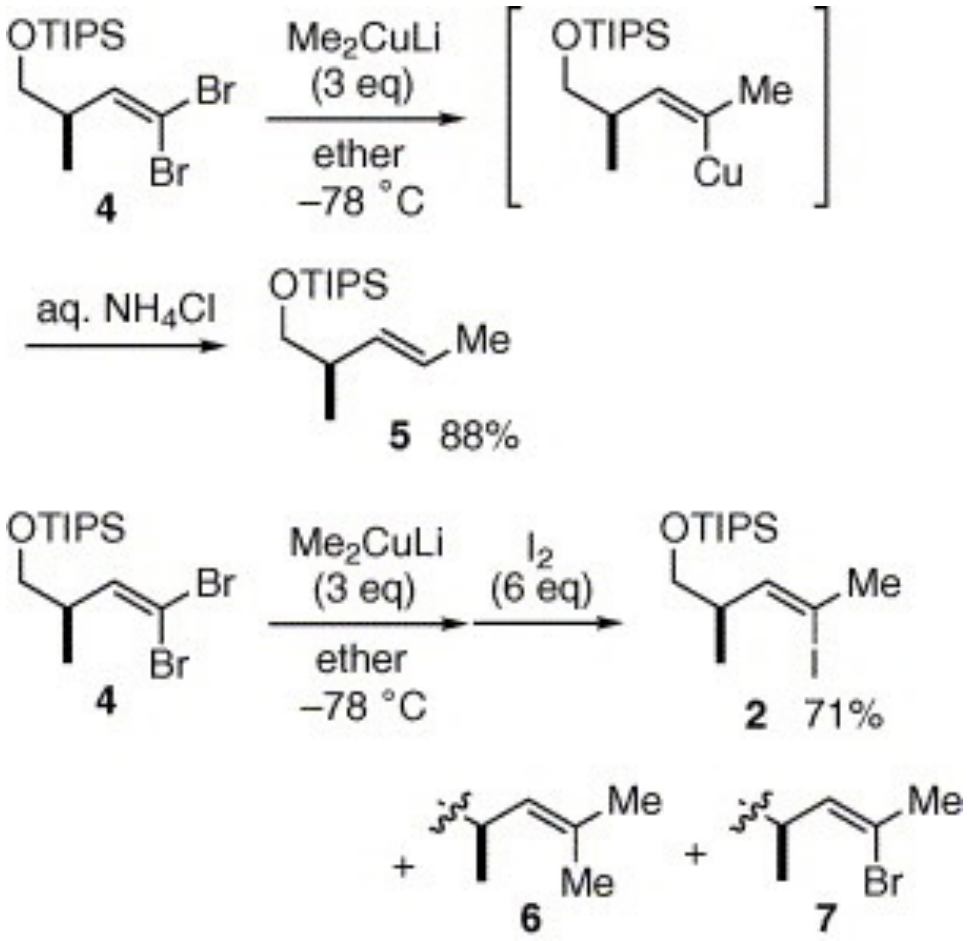




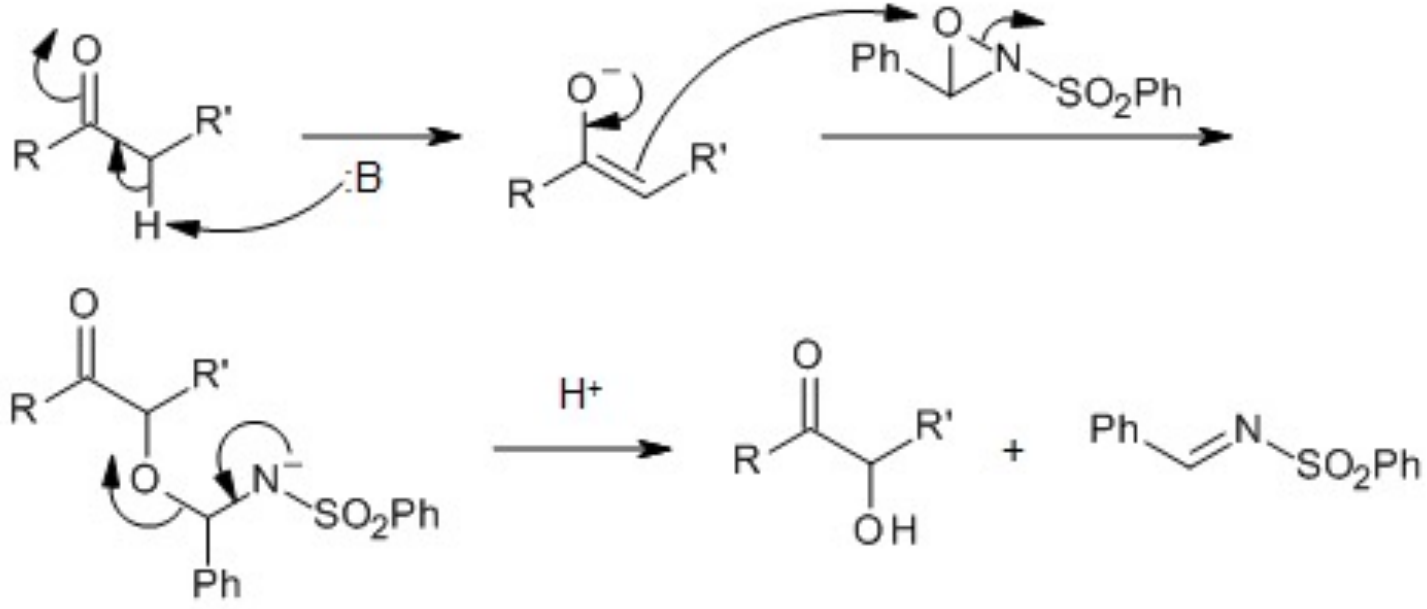
Martin sulfurane



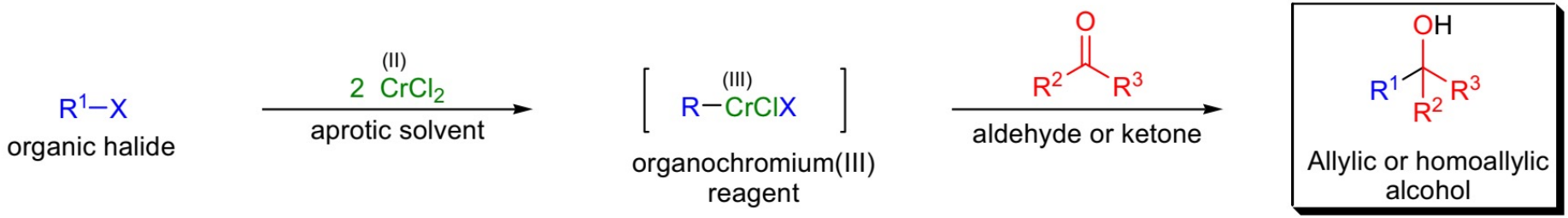
22 Tanino and Myashita Method



davis's oxaziridine

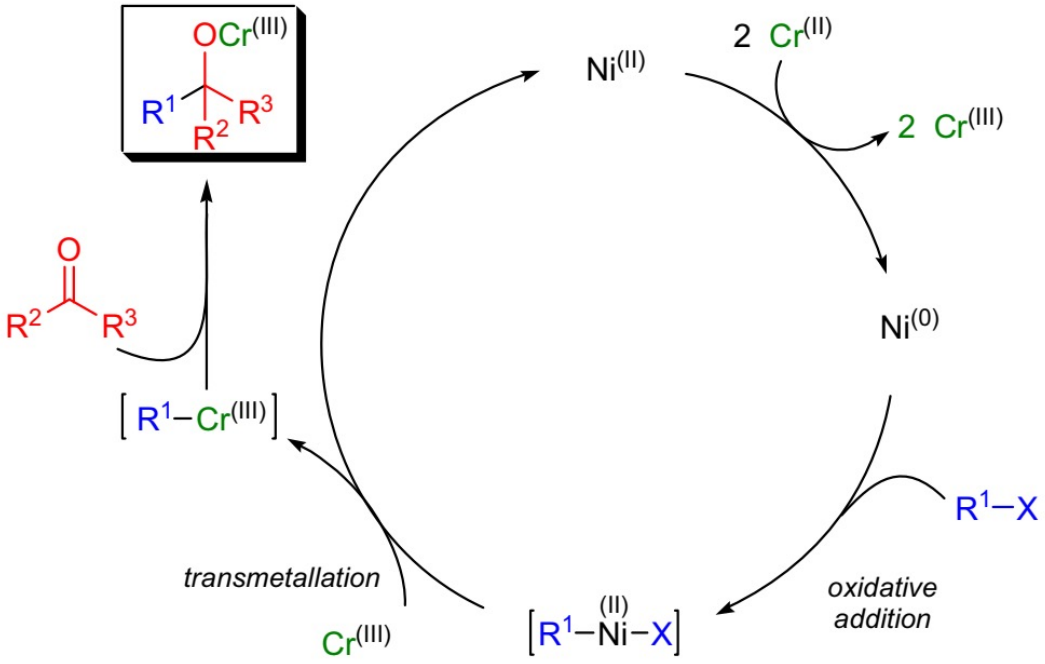


NHK

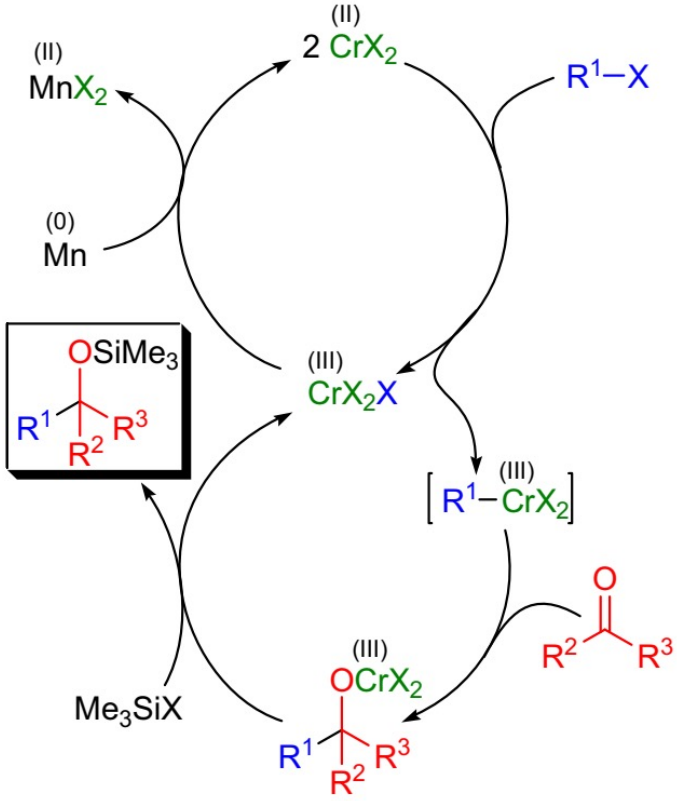


R^1 = alkenyl, aryl, allyl, vinyl, propargyl, alkynyl, allenyl; X = Cl, Br, I, OTf, etc.; R^2, R^3 = alkyl, aryl, alkenyl, H;
solvent: DMF, DMSO, THF

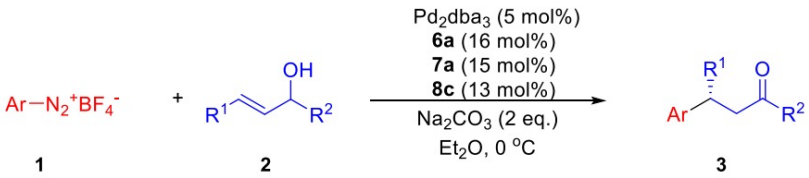
$Ni^{(II)}$-catalyzed process:

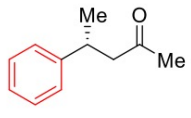


Chromium-catalyzed process:

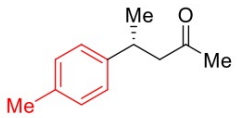


Scheme 3. Substrate Scope[a]

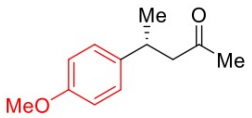




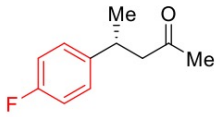
3a, 75%, 95:5 er



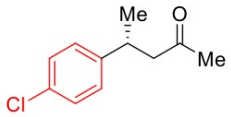
3b, 76%, 94.5:5.5 er



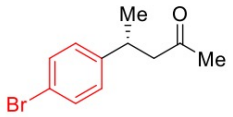
3c, 71%, 95:5 er



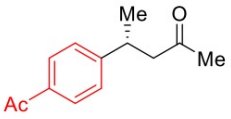
3d, 69%, 93.5:6.5 er



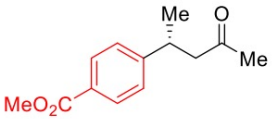
3e, 71%, 95.5:4.5 er



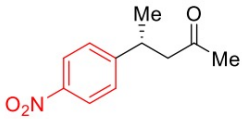
3f, 58%, 94.5:5.5 er



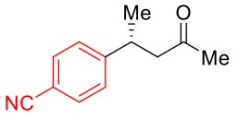
3g, 76%, 94:6 er
1 mmol scale: 73%, 94:6 er



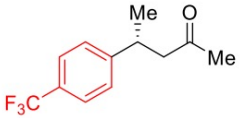
3h, 68%, 96:4 er



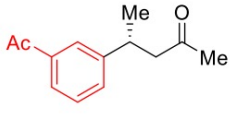
3i, 80%, 93:7 er



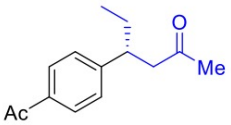
3j, 66%, 92:8 er



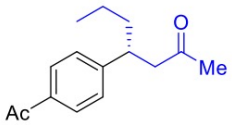
3k, 51%, 93.5:6.5 er



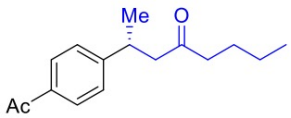
3l, 76%, 91.5:8.5 er



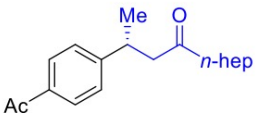
3m, 75%, 90.5:9.5 er



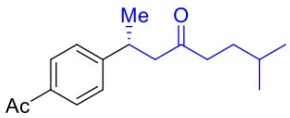
3n, 67%, 89:11 er



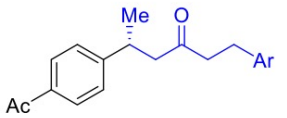
3o, 72%, 95.5:4.5 er



3p, 76%, 97:3 er



3q, 44%, 96.5:3.5 er[b]



4-MeO-C_6H_4
3r, 66%, 93:7 er[b]

Br2, NaOH

Me4Sn