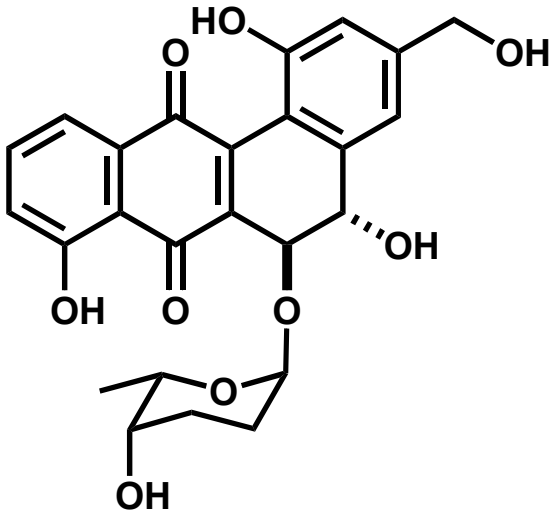
Total Synthesis of TAN-1085

2019.11.02. Literature Seminar
B4 Yuma Komori

Contents

TAN-1085



TAN-1085

Isolation: *Streptomyces* sp. S-11106[1), 2)]

Biological activity: angiogenesis inhibition, aromatase inhibition[1), 2)]

Structural features: curved tetracyclic chromophore, trans vicinal diol one of which is glycosylated[2)]

Total synthesis: Suzuki (2004 (racemic), 2009)[2), 3)], Shi (2019)[4)]

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1) Kanamaru, T.; Nozaki, Y.; Muroi, M. (Kokai Tokkyo Koho). JP 02-289-532/1990, **1991** [*Chem. Abstr.* **1991**, *115*, 47759n].
2) Ohmori, K.; Mori, K.; Ishikawa, Y.; Tsuruta, H.; Kuwahara, S.; Harada, N.; Suzuki, K. *Angew. Chem. Int. Ed.* **2004**, *43*, 3167.
3) Mori, K.; Ohmori, K.; Suzuki, K. *Angew. Chem. Int. Ed.* **2009**, *48*, 5633.
4) Fan, J.; Yao, Q. J.; Liu, Y. H.; Liao, G.; Zhang, S.; Shi, B. F. *Org. Lett.* **2019**, *21*, 3352

Introduction of Prof. Suzuki and Shi

Prof. Keisuke Suzuki

1978 B.S. @University of Tokyo
1983 Ph.D @University of Tokyo (Prof. Mukaiyama)
1983 Assistant professor @Keio University (Prof. Tsuchihashi)
1989 Associate professor @Keio University
1994 Professor @Keio University
1996-Professor @Tokyo Institute of Technology

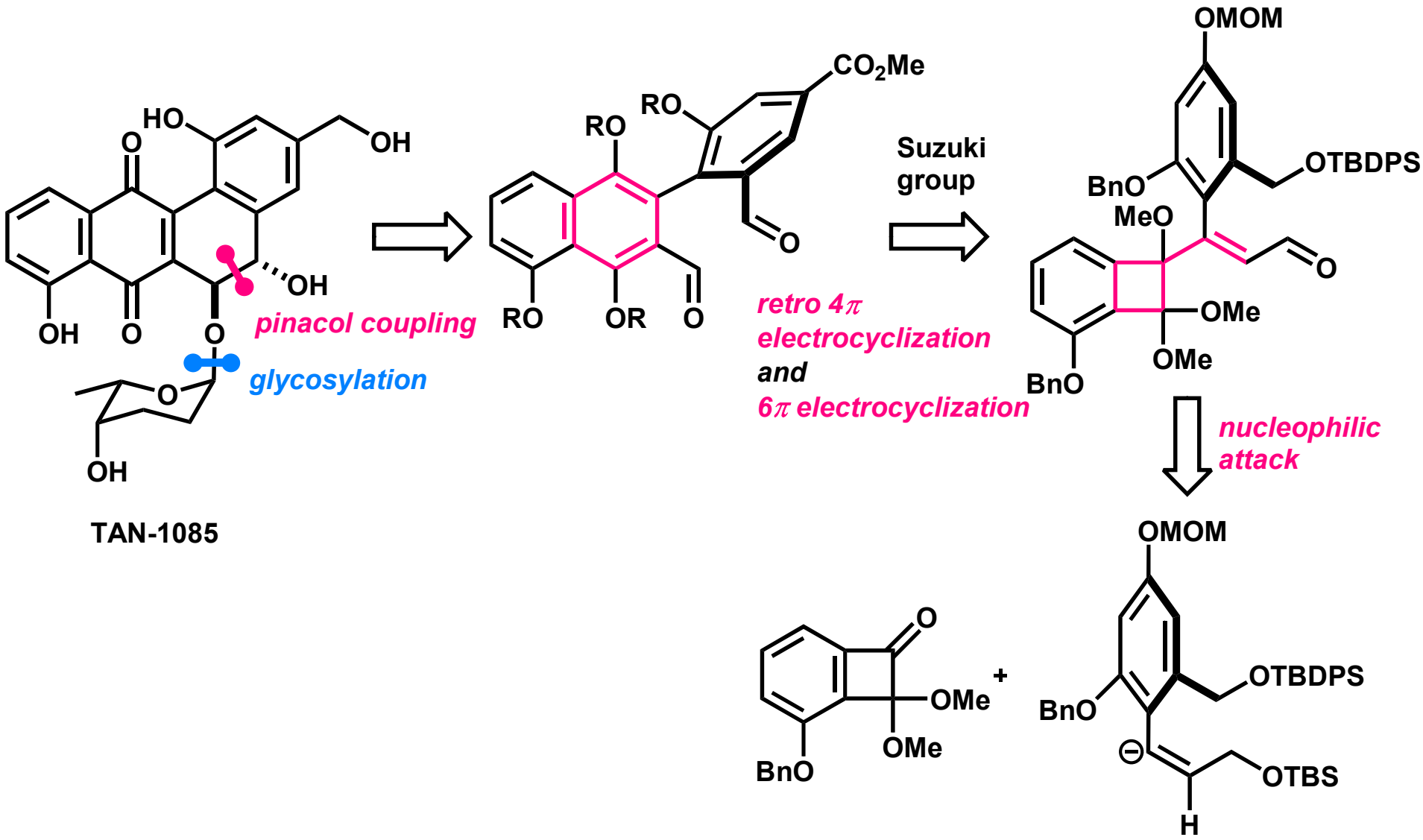
Research topic: total synthesis, reaction development

Prof. Bing-Feng Shi
2001 B.S. @Nankai University (Prof. Ji-Ben Meng)
2006 Ph.D @Shanghai Institute of Organic Chemistry (Prof. Biao Yu)
2006 Postdoctoral fellow @UC San Diego (Prof. Michael S. VanNieuwenhze)
2007 Research associate @The scripps Research Institute (Prof. Jin-Quan Yu)
2010 Tenure-track Professor @Zhejiang University
2015- Professor @Zhejiang University

Research topic: C-H activation, total synthesis

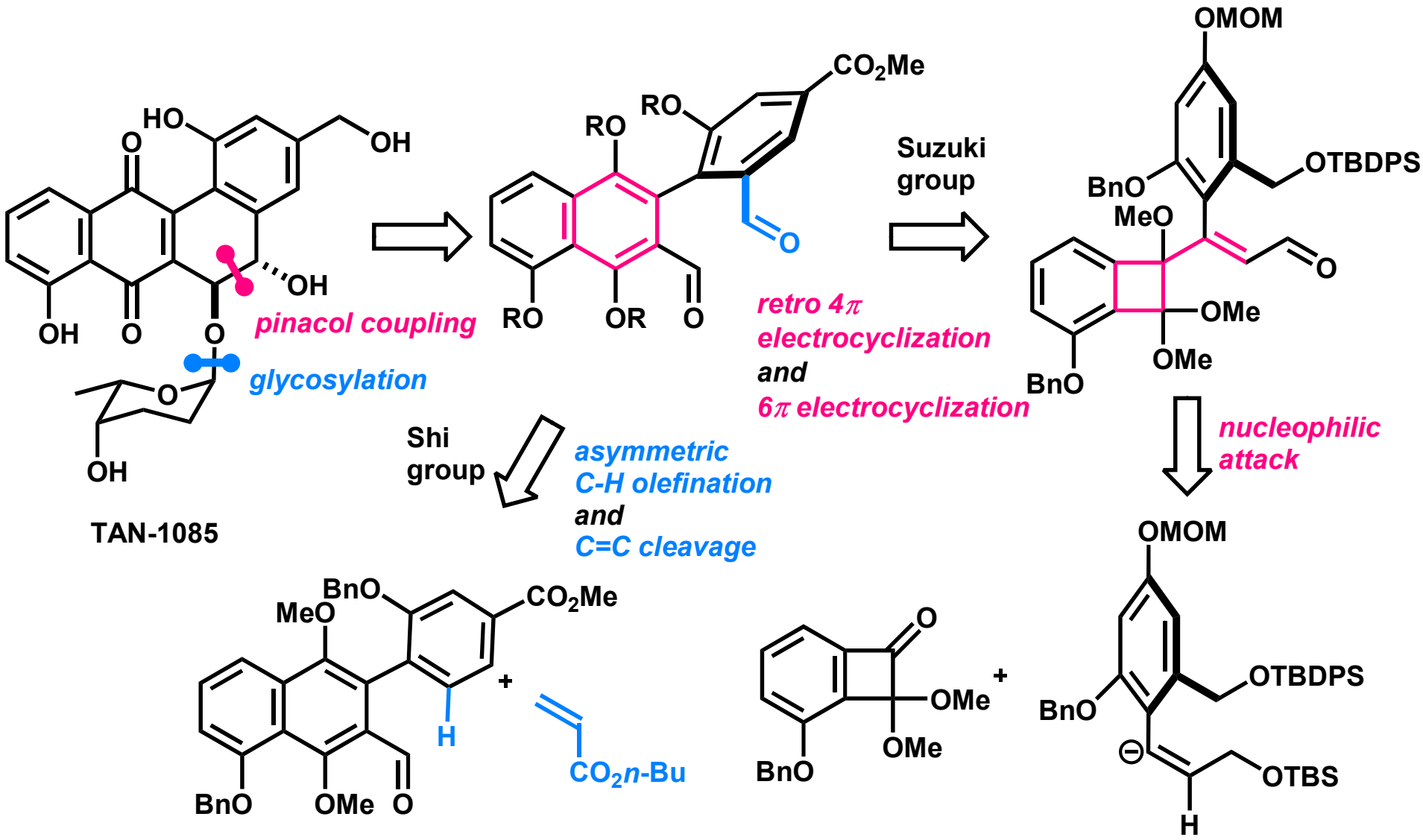
1) http://www.org-synth.chem.sci.titech.ac.jp/suzukilab/?page_id=7
2) https://person.zju.edu.cn/en/bfshi

Retrosynthetic Analysis of 2 Groups



1) Mori, K.; Ohmori, K.; Suzuki, K. *Angew. Chem. Int. Ed.* **2009**, *48*, 5633.
2) Ohmori, K.; Mori, K.; Ishikawa, Y.; Tsuruta, H.; Kuwahara, S.; Harada, N.; Suzuki, K. *Angew. Chem. Int. Ed.* **2004**, *43*, 3167.
3) Fan, J.; Yao, Q.-J.; Liu, Y.-H.; Liao, G.; Zhang, S.; Shi, B.-F. *Org. Lett.* **2019**, *21,* 3352.

Retrosynthesis of 2 Groups



1) Mori, K.; Ohmori, K.; Suzuki, K. *Angew. Chem. Int. Ed.* **2009**, *48*, 5633.
2) Ohmori, K.; Mori, K.; Ishikawa, Y.; Tsuruta, H.; Kuwahara, S.; Harada, N.; Suzuki, K. *Angew. Chem. Int. Ed.* **2004**, *43*, 3167.
3) Fan, J.; Yao, Q.-J.; Liu, Y.-H.; Liao, G.; Zhang, S.; Shi, B.-F. *Org. Lett.* **2019**, *21,* 3352.

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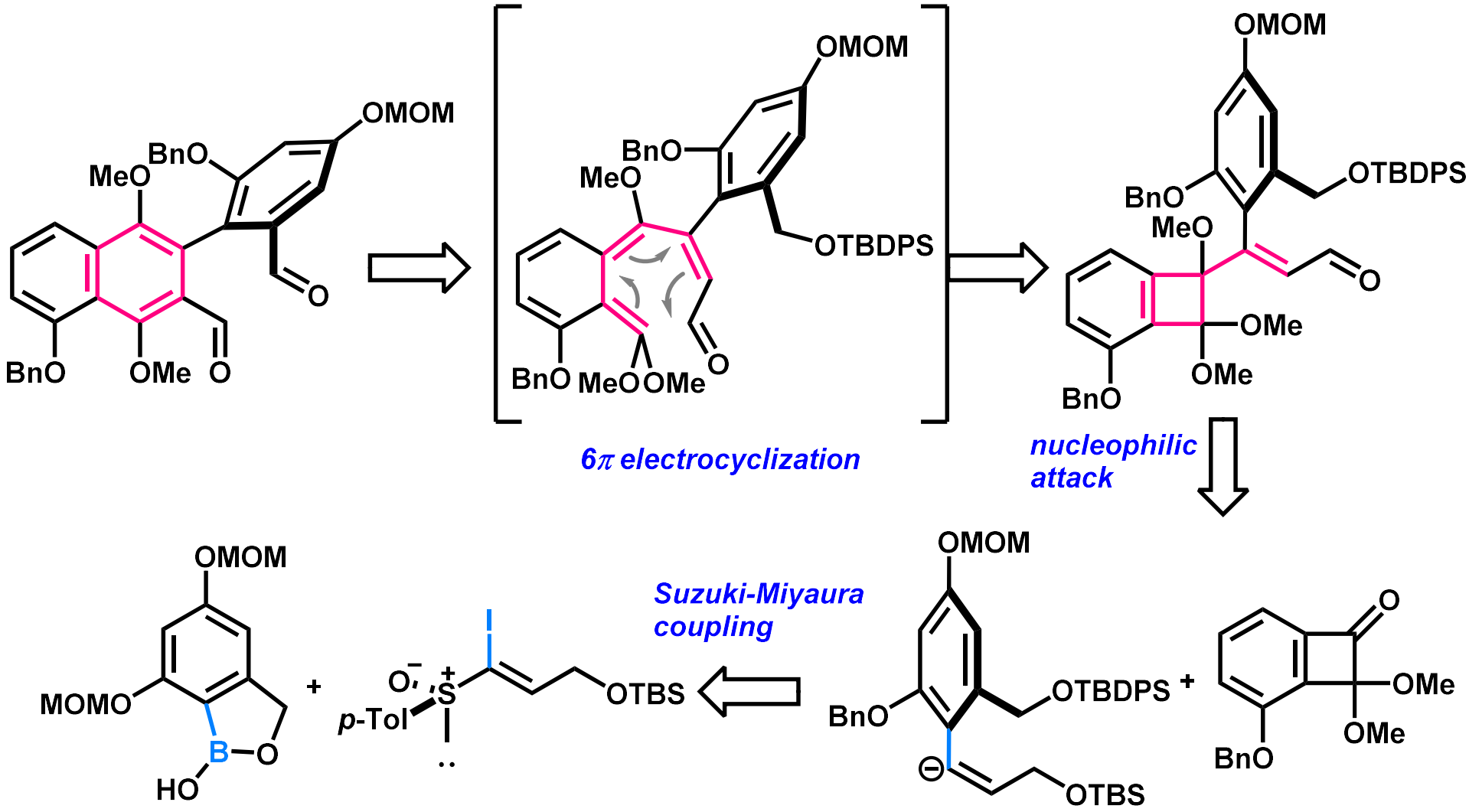
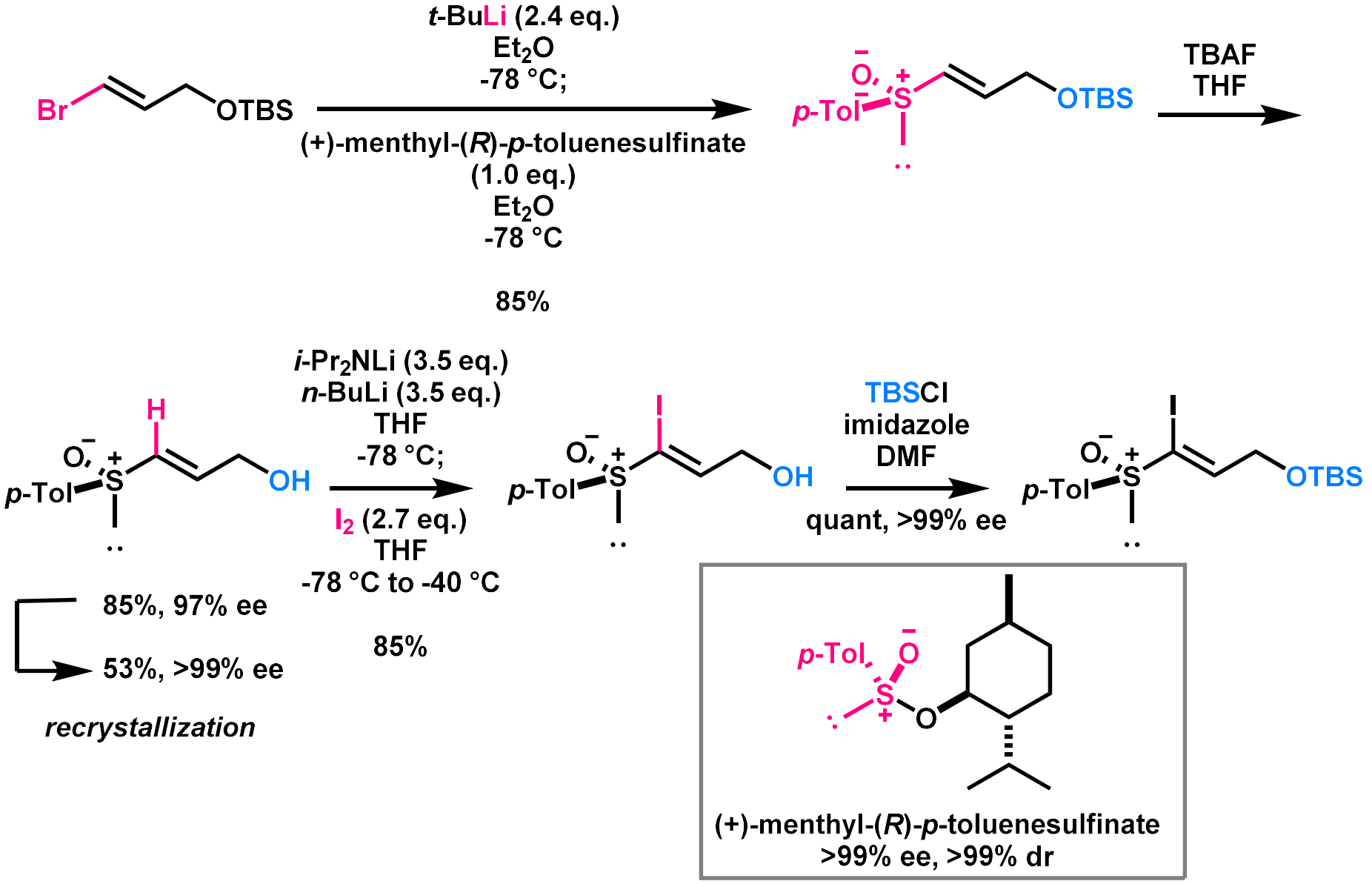
Retrosynthesis



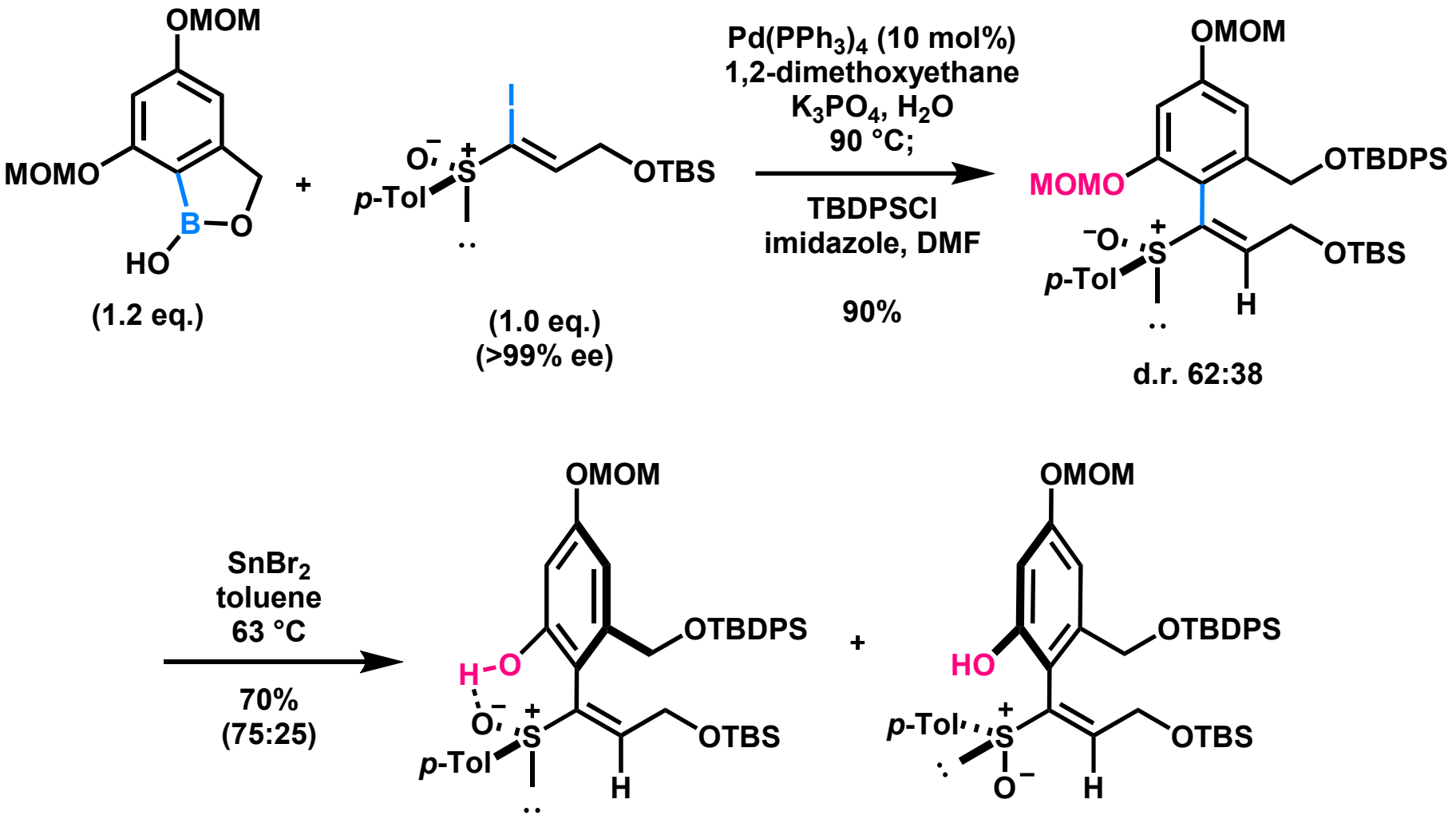
1) Mori, K.; Ohmori, K.; Suzuki, K. *Angew. Chem. Int. Ed.* **2009**, *48*, 5633.
2) Ohmori, K.; Mori, K.; Ishikawa, Y.; Tsuruta, H.; Kuwahara, S.; Harada, N.; Suzuki, K. *Angew. Chem. Int. Ed.* **2004**, *43*, 3167.

Synthesis of Vinyl Sulfoxide



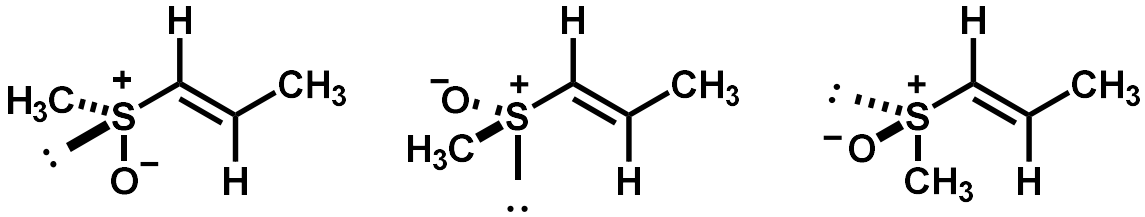
1) Mori, K.; Ohmori, K.; Suzuki, K. *Angew. Chem. Int. Ed.* **2009**, *48*, 5633.

Installation of Axial Chirality

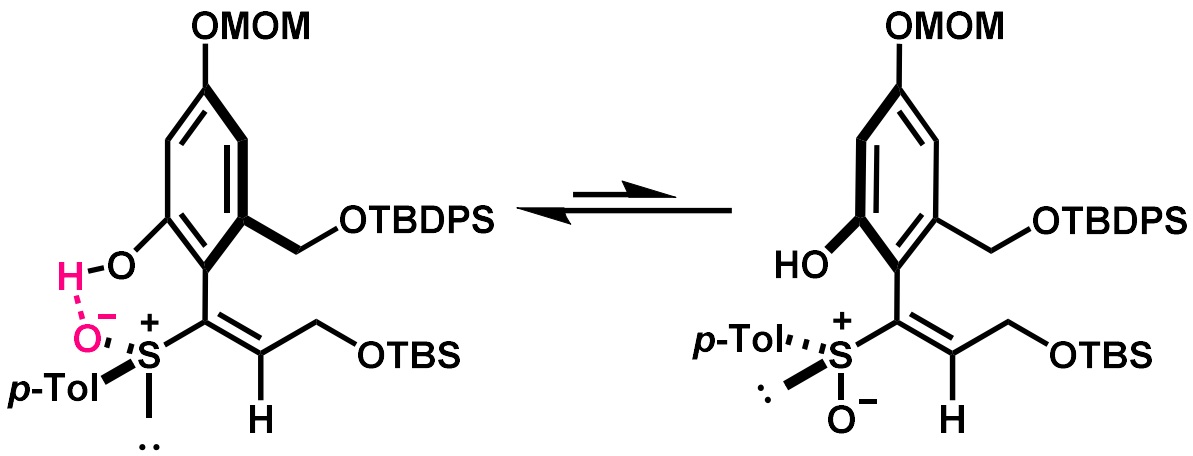


1) Mori, K.; Ohmori, K.; Suzuki, K. *Angew. Chem. Int. Ed.* **2009**, *48*, 5633.

Stereoselectivity

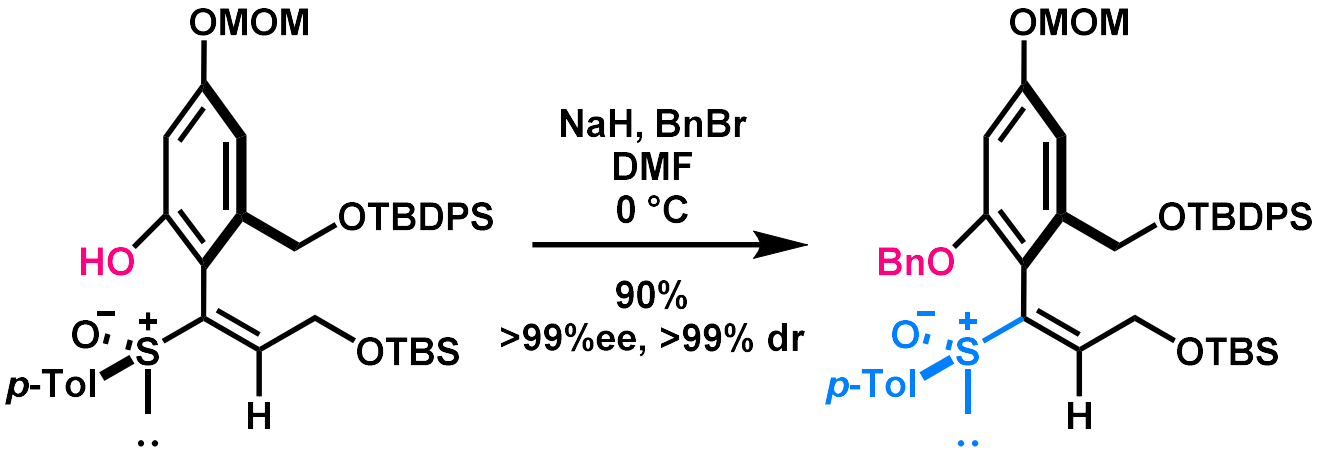


Relative energy (kcal mol^{-1})	0	+1.2	+5.4

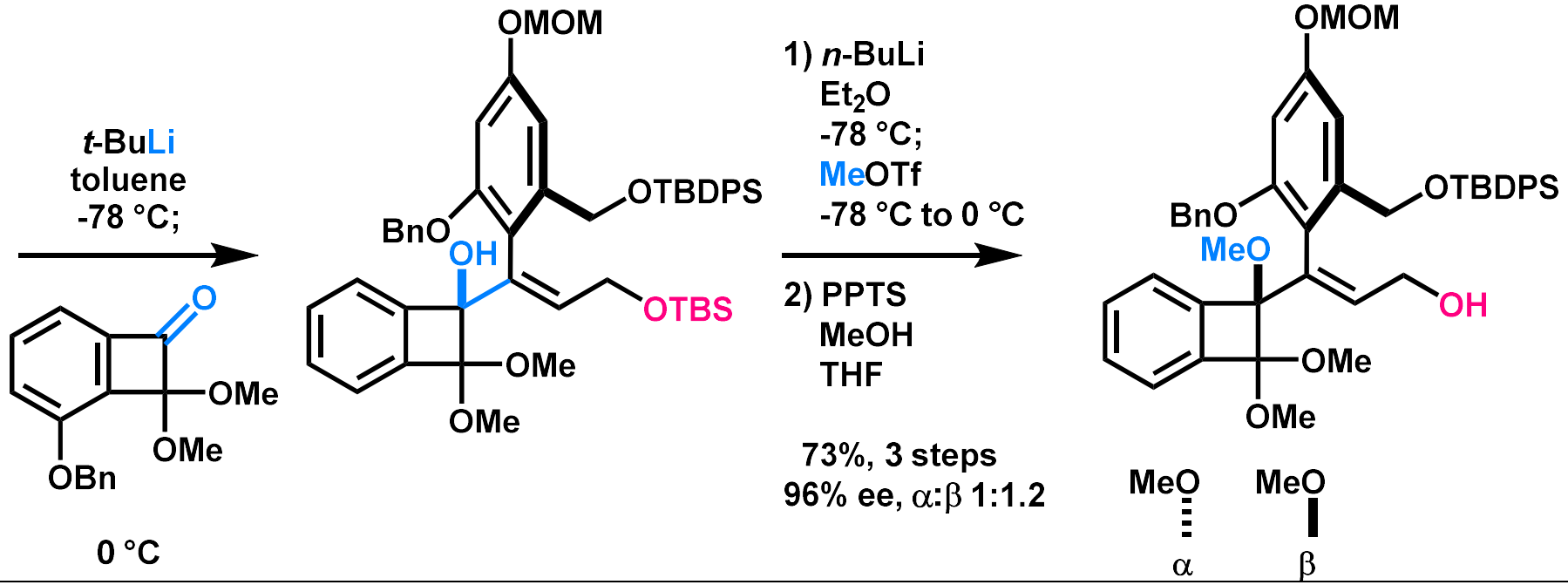


1) Mori, K.; Ohmori, K.; Suzuki, K. *Angew. Chem. Int. Ed.* **2009**, *48*, 5633.

Synthesis of Precursor of Pericyclic Reaction

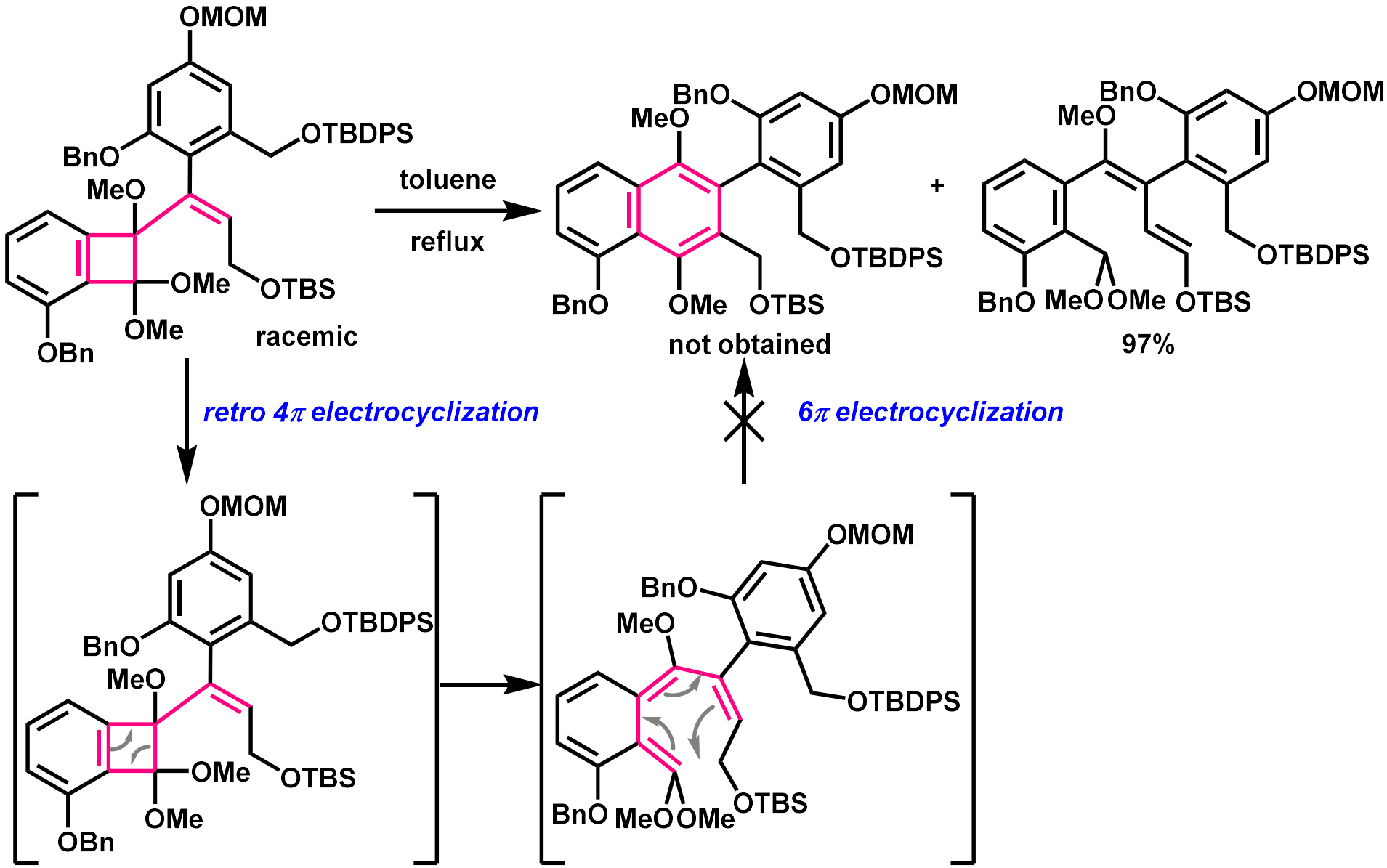


>99%ee, >99% dr



1) Mori, K.; Ohmori, K.; Suzuki, K. *Angew. Chem. Int. Ed.* **2009**, *48*, 5633.

Previous Study of Pericyclic Reaction



1) Ohmori, K.; Mori, K.; Ishikawa, Y.; Tsuruta, H.; Kuwahara, S.; Harada, N.; Suzuki, K. *Angew. Chem. Int. Ed.* **2004**, *43*, 3167.

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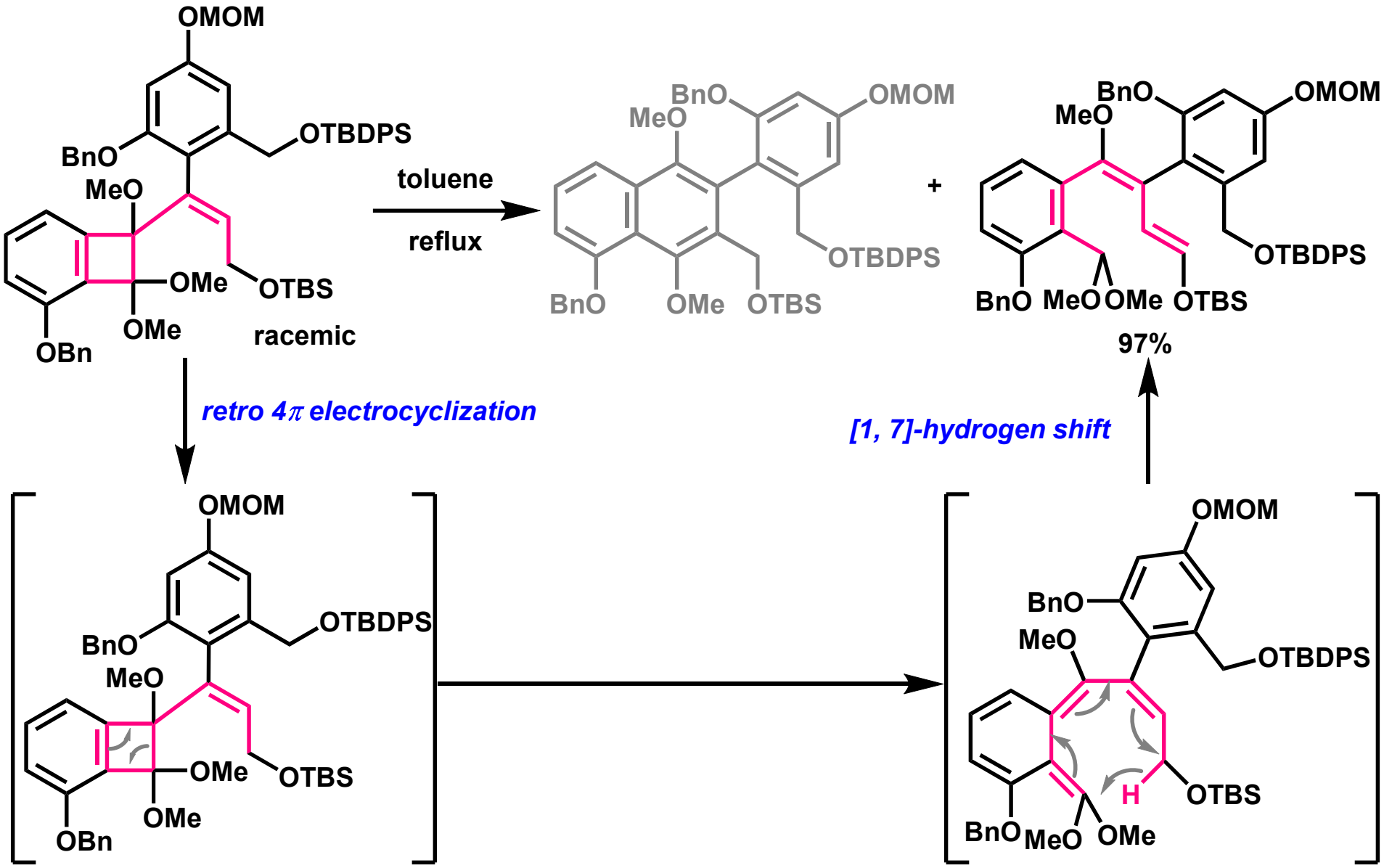
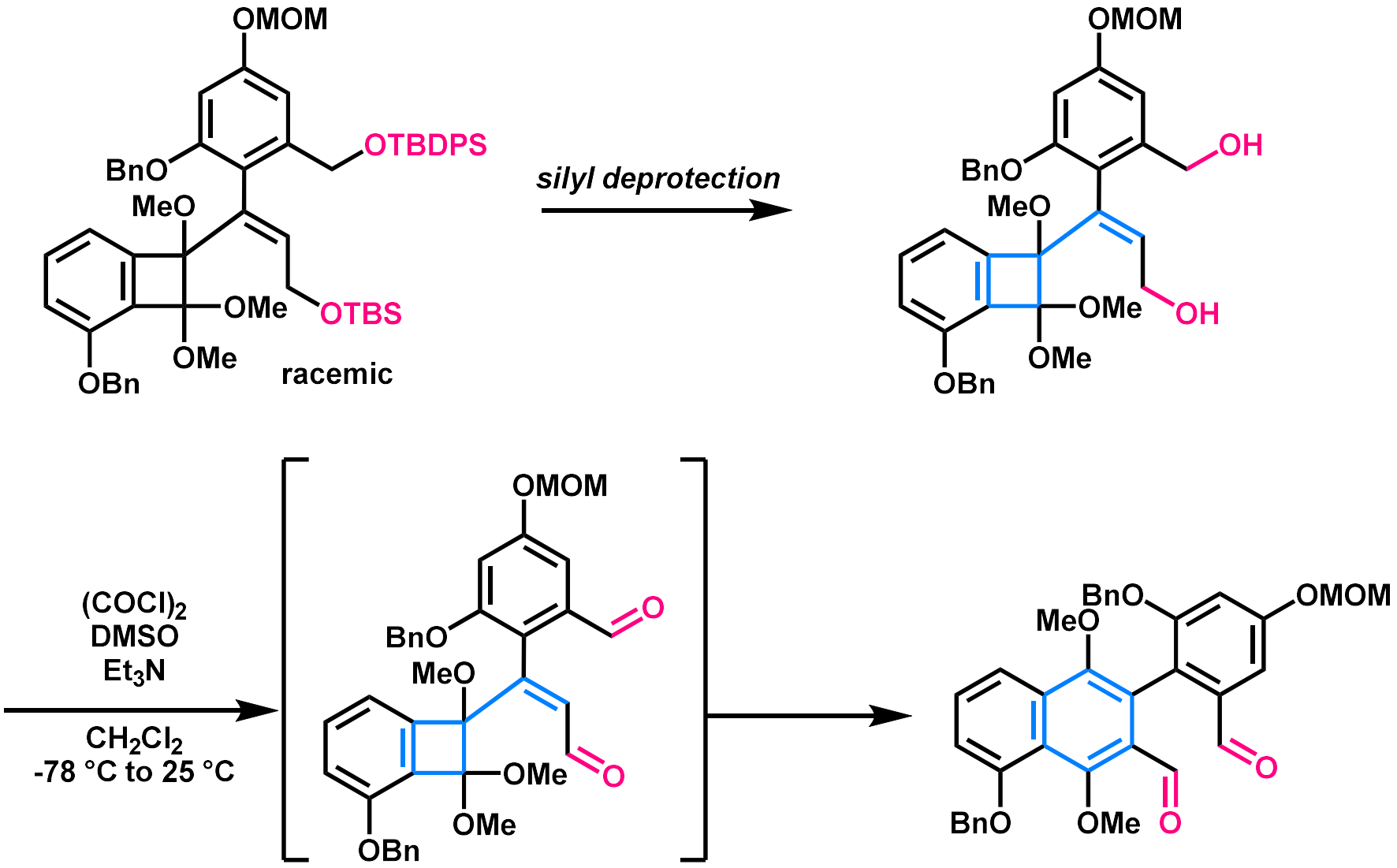


1) Ohmori, K.; Mori, K.; Ishikawa, Y.; Tsuruta, H.; Kuwahara, S.; Harada, N.; Suzuki, K. *Angew. Chem. Int. Ed.* **2004**, *43*, 3167.

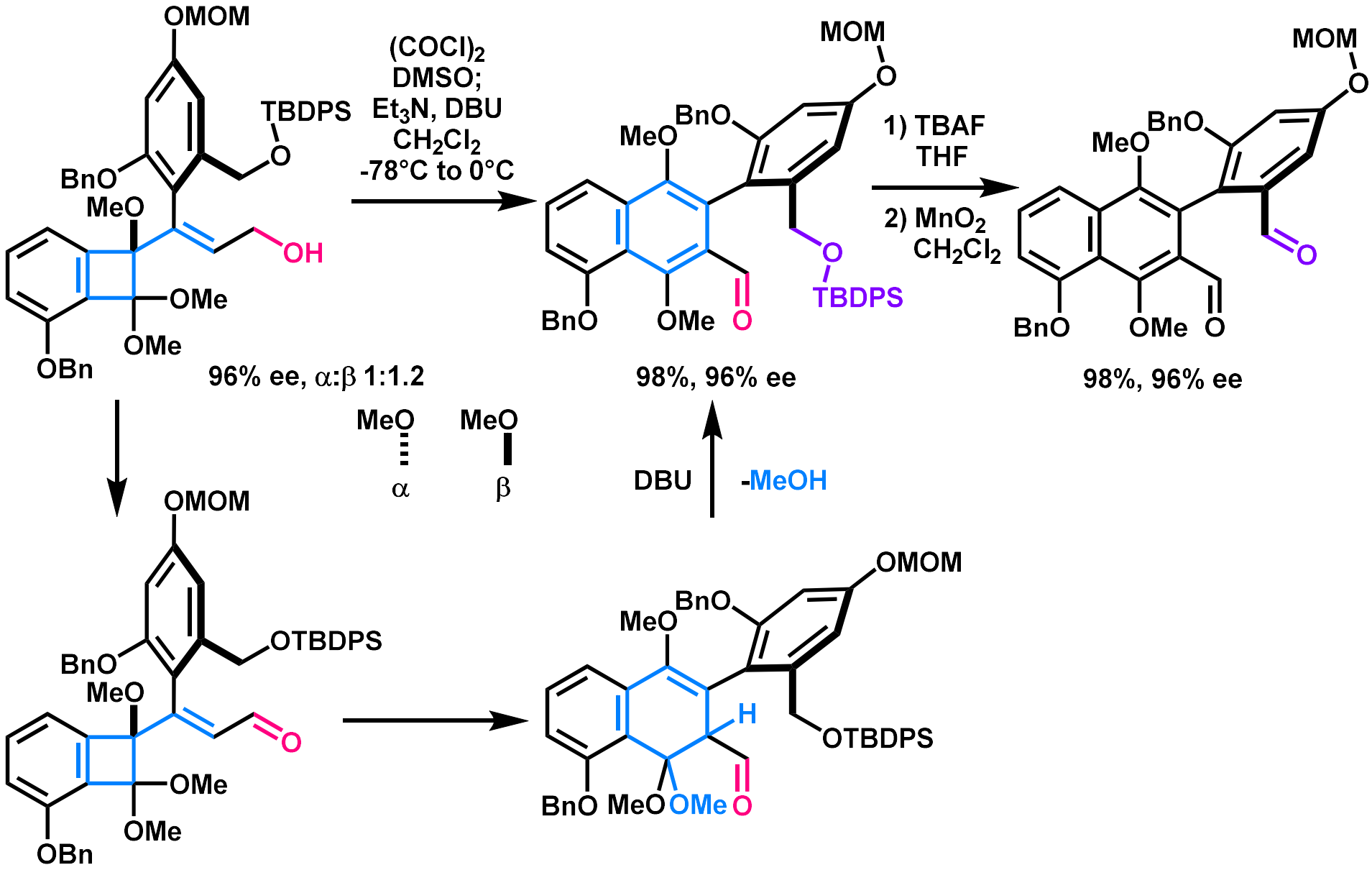
Swern Oxidation to Repress Side Reaction



***Details of these reactions' conditions were not written on the paper.**

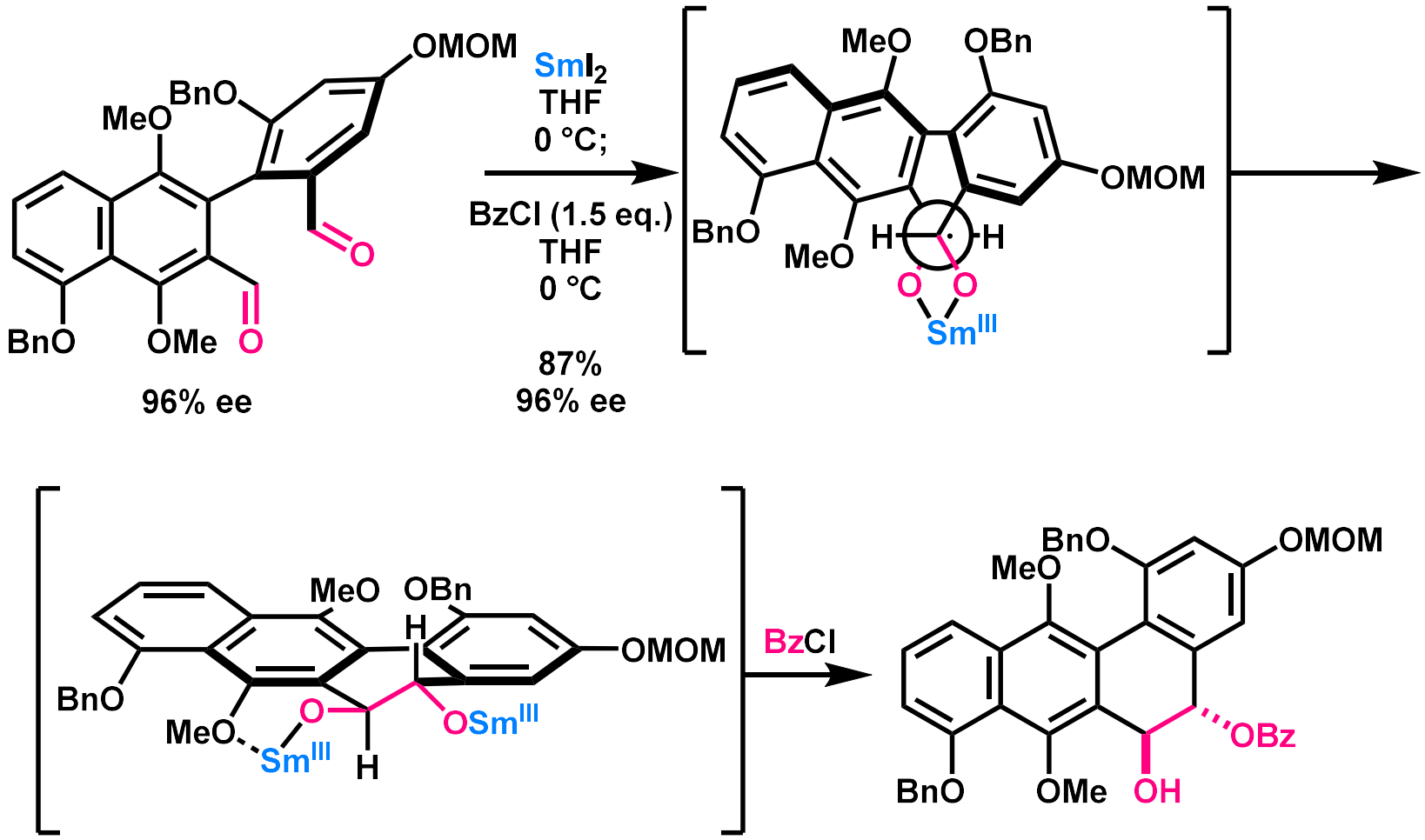
1) Ohmori, K.; Mori, K.; Ishikawa, Y.; Tsuruta, H.; Kuwahara, S.; Harada, N.; Suzuki, K. *Angew. Chem. Int. Ed.* **2004**, *43*, 3167.

Swern Oxidation of Chiral Substrate



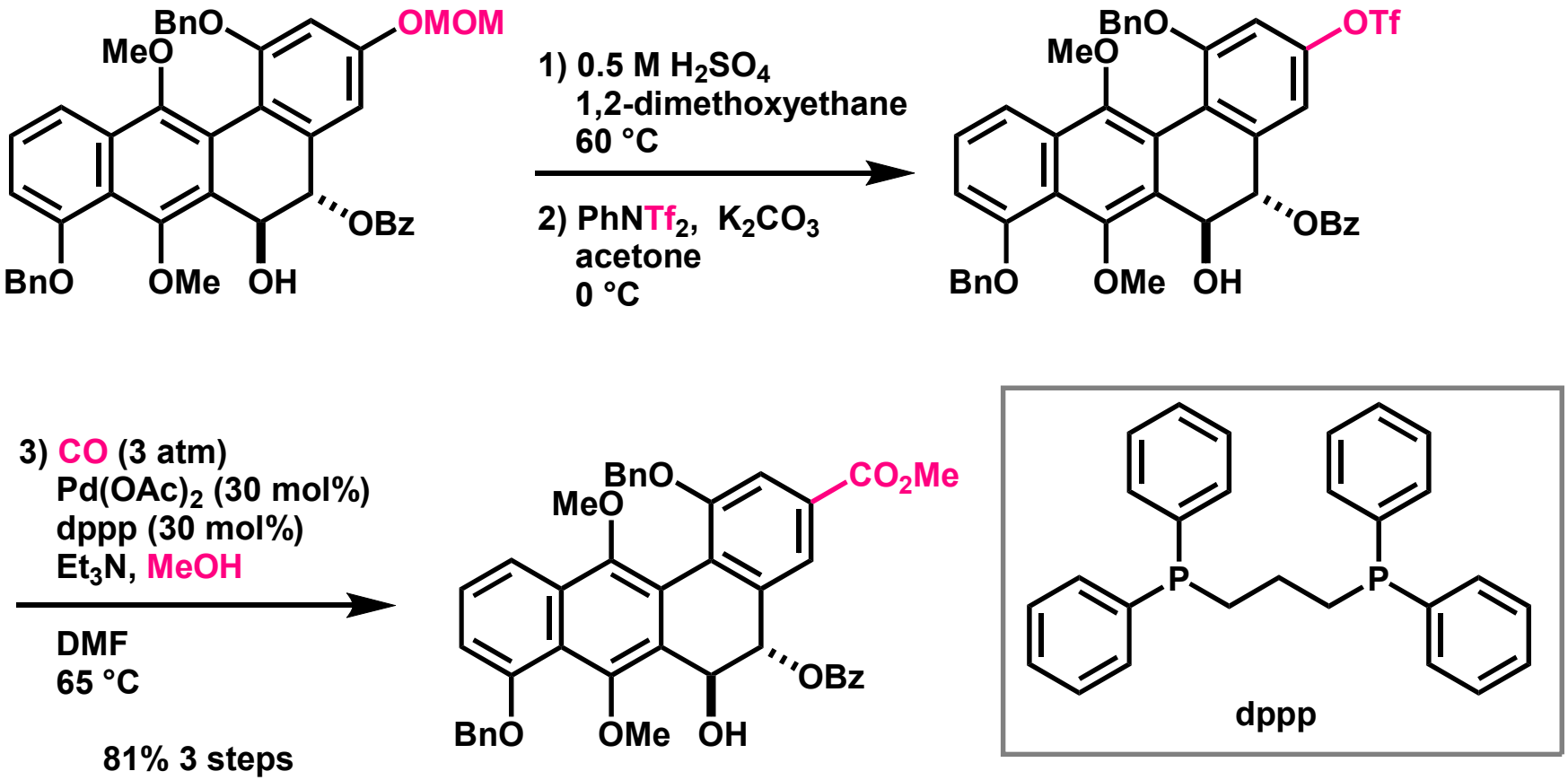
1) Mori, K.; Ohmori, K.; Suzuki, K. *Angew. Chem. Int. Ed.* **2009**, *48*, 5633.

Pinacol Coupling



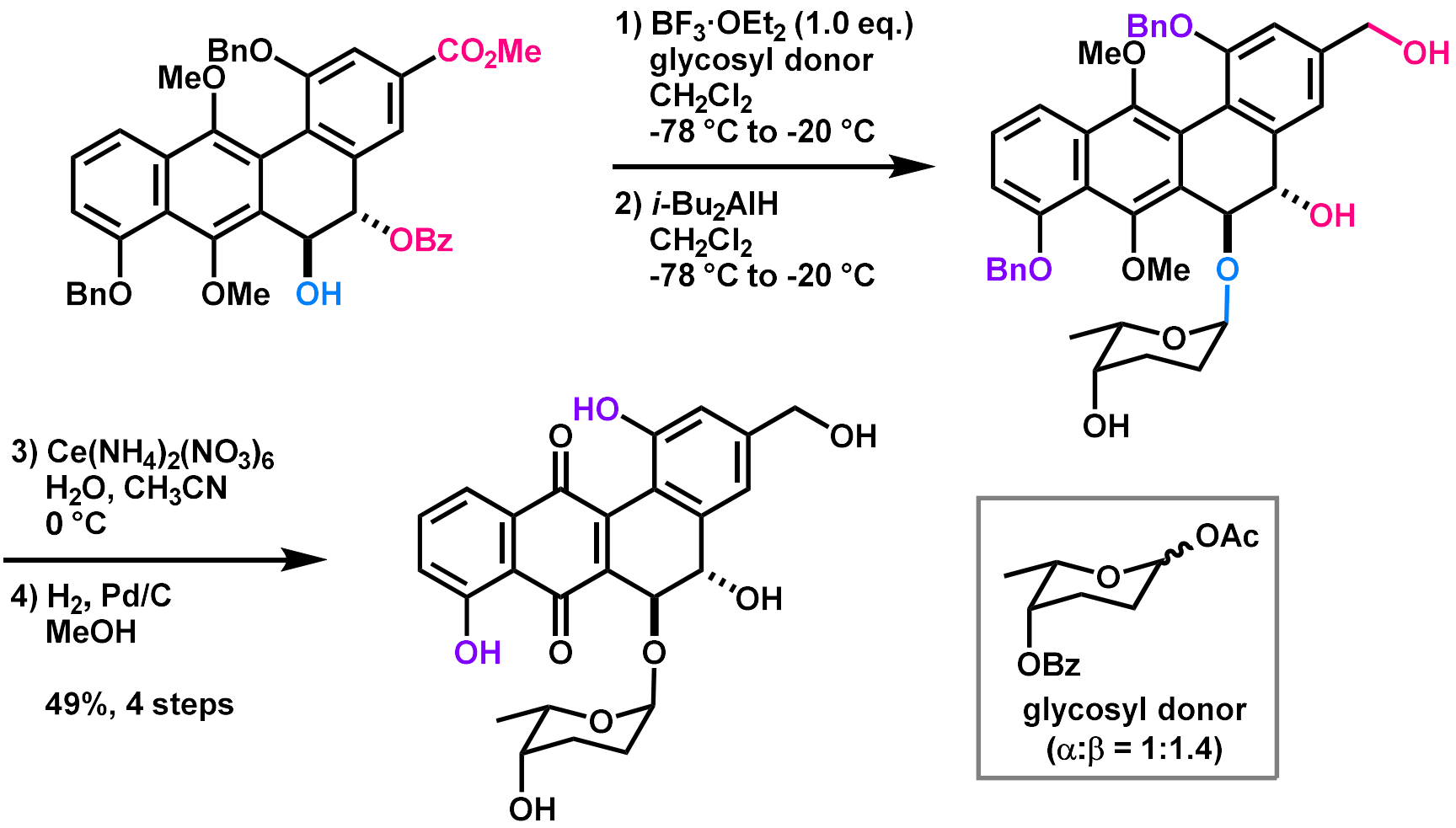
1) Mori, K.; Ohmori, K.; Suzuki, K. *Angew. Chem. Int. Ed.* **2009**, *48*, 5633.

Synthesis of Ester by Carboxylative Coupling



1) Mori, K.; Ohmori, K.; Suzuki, K. *Angew. Chem. Int. Ed.* **2009**, *48*, 5633.

Total Synthesis of TAN-1085



1) Mori, K.; Ohmori, K.; Suzuki, K. *Angew. Chem. Int. Ed.* **2009**, *48*, 5633.

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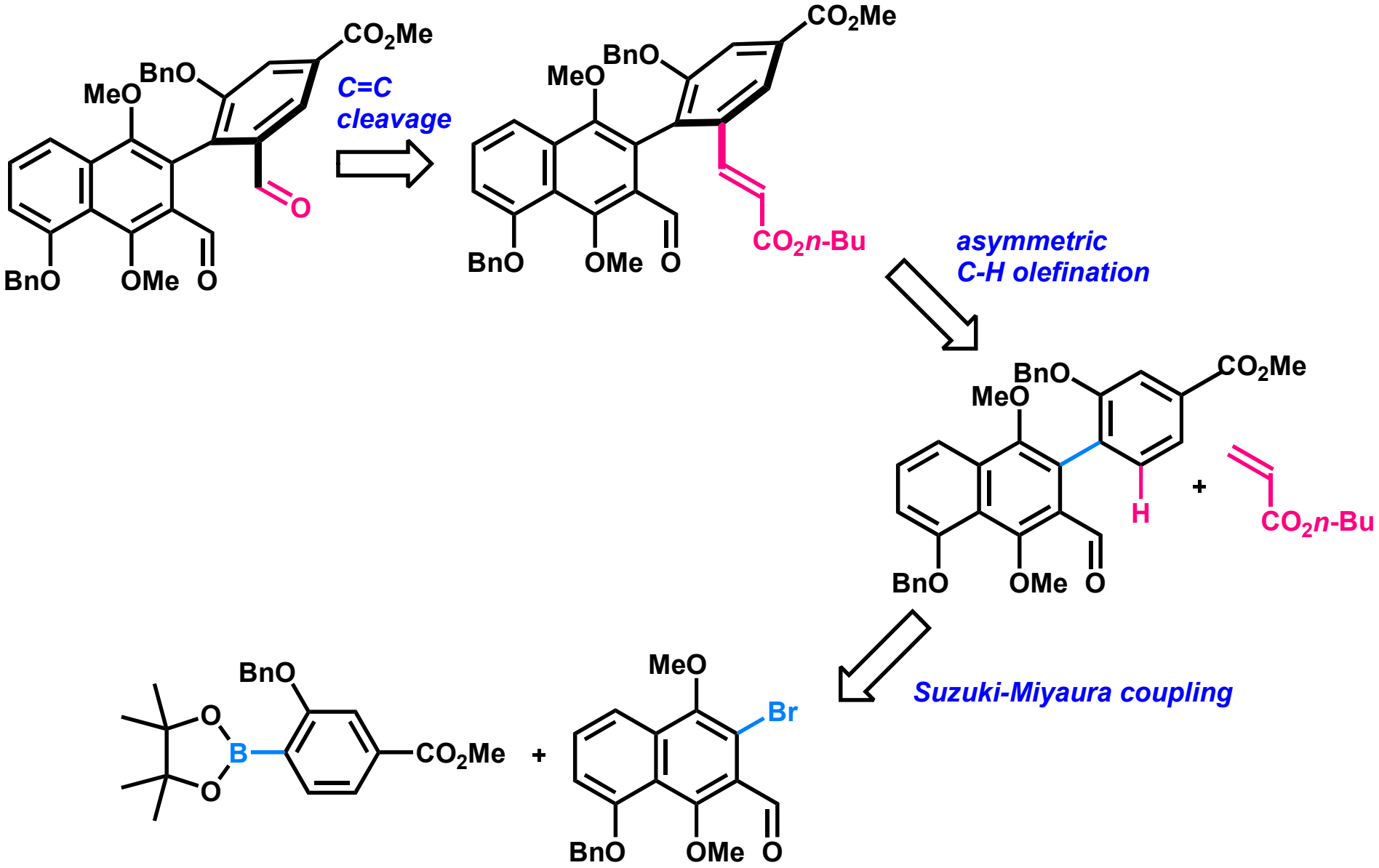
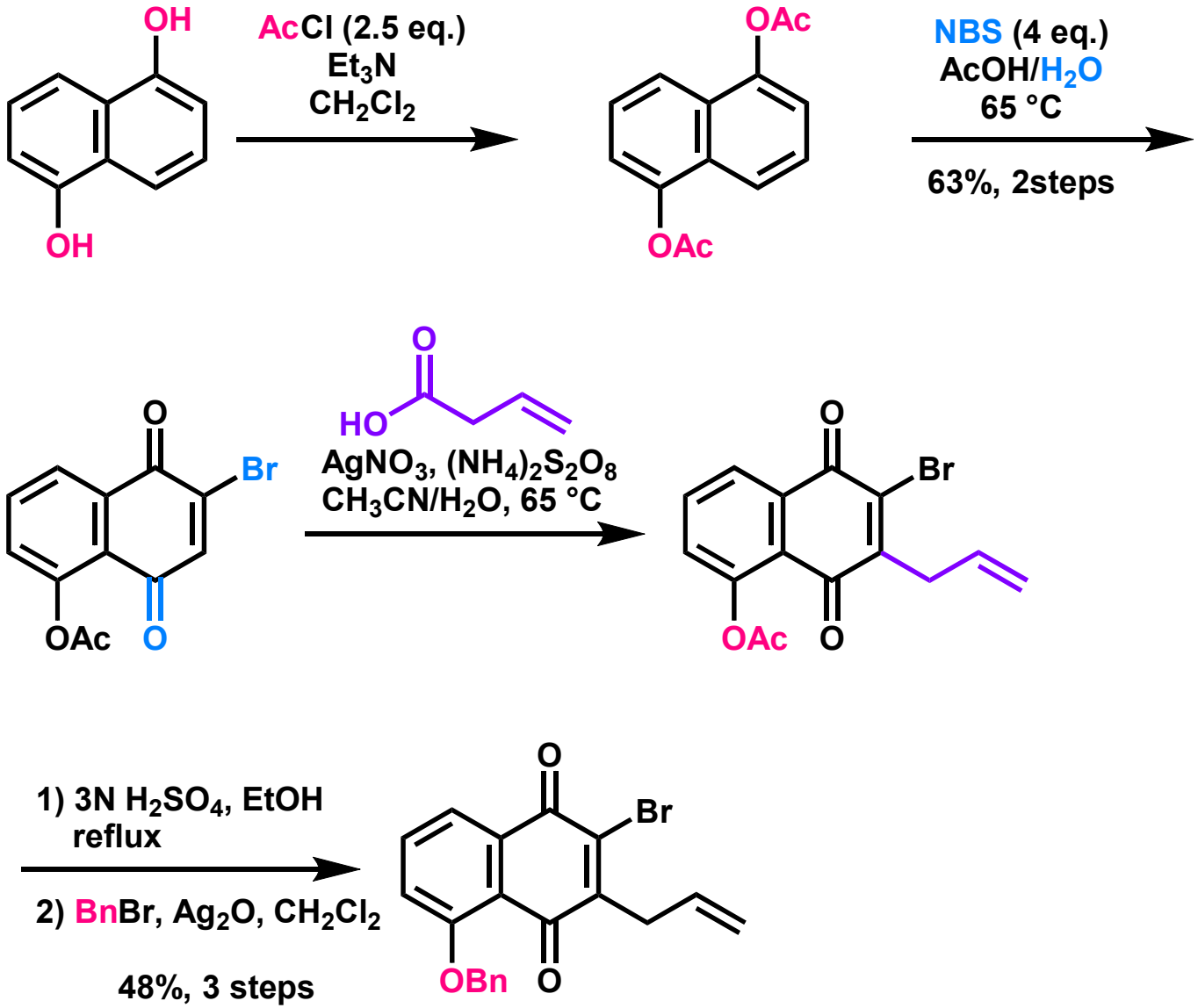


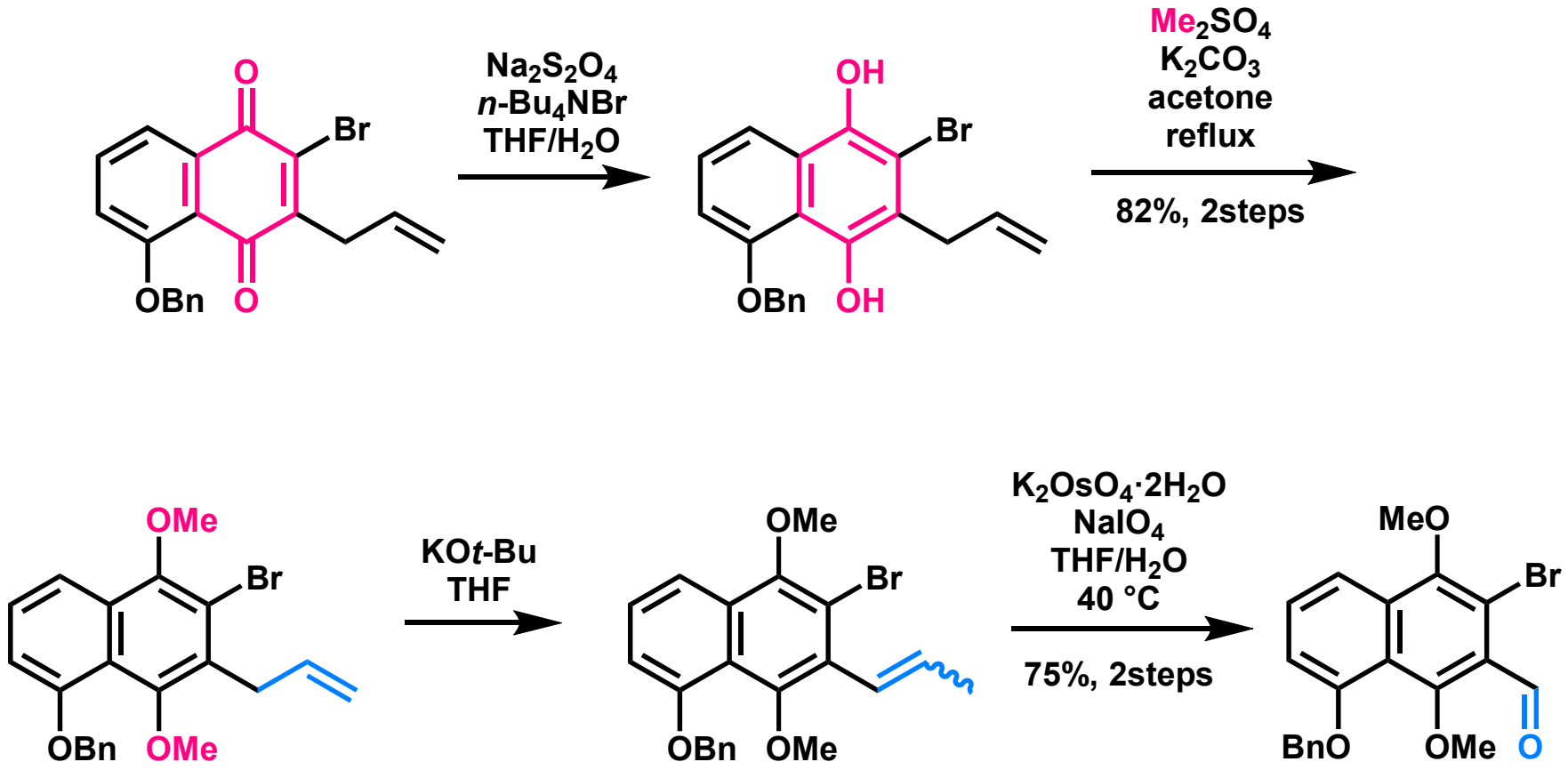
1) Fan, J.; Yao, Q.-J.; Liu, Y.-H.; Liao, G.; Zhang, S.; Shi, B.-F. *Org. Lett.* **2019**, *21,* 3352.

Synthesis of Naphthoquinone



1) Fan, J.; Yao, Q.-J.; Liu, Y.-H.; Liao, G.; Zhang, S.; Shi, B.-F. *Org. Lett.* **2019**, *21,* 3352.

Synthesis of Aryl Bromide



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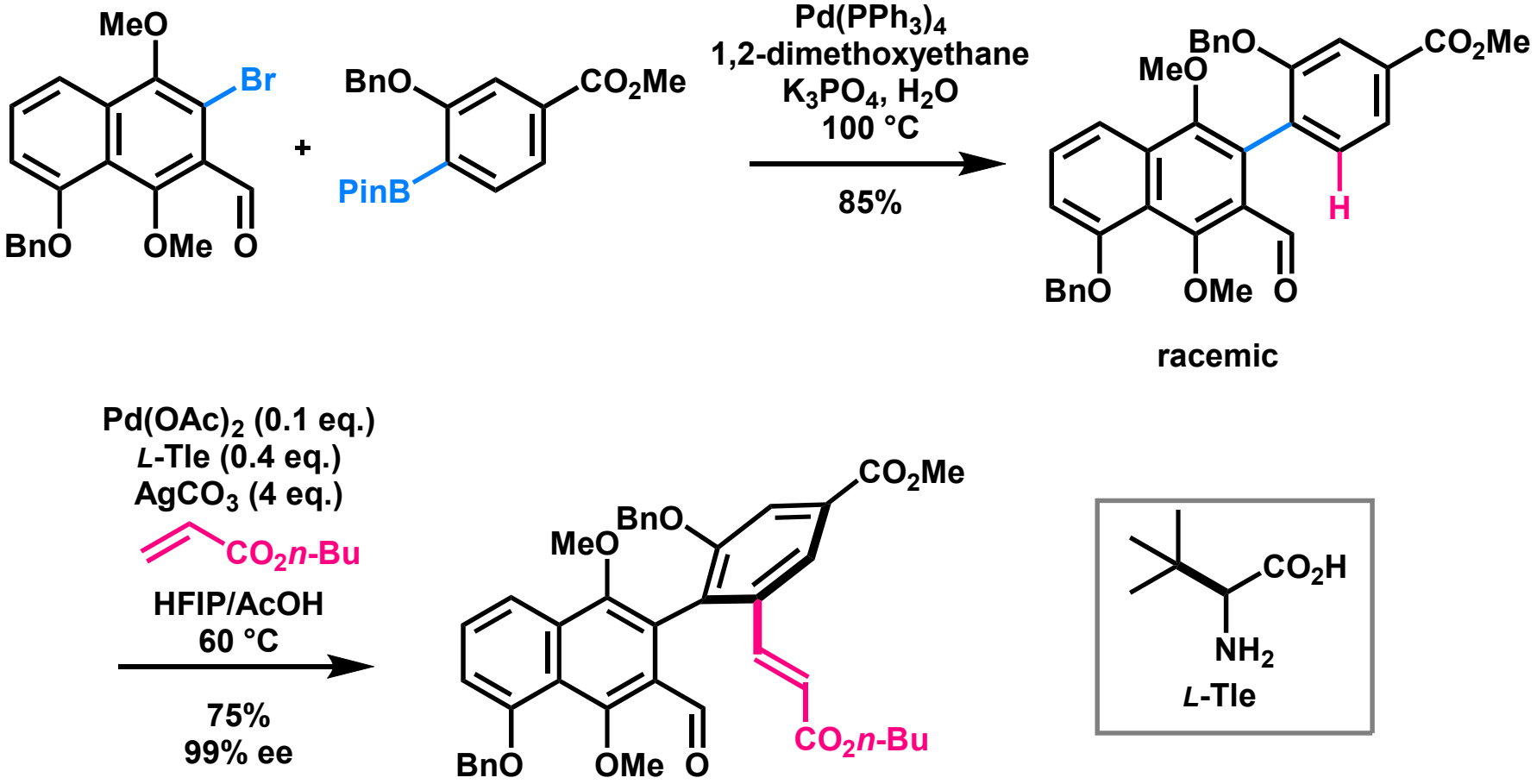
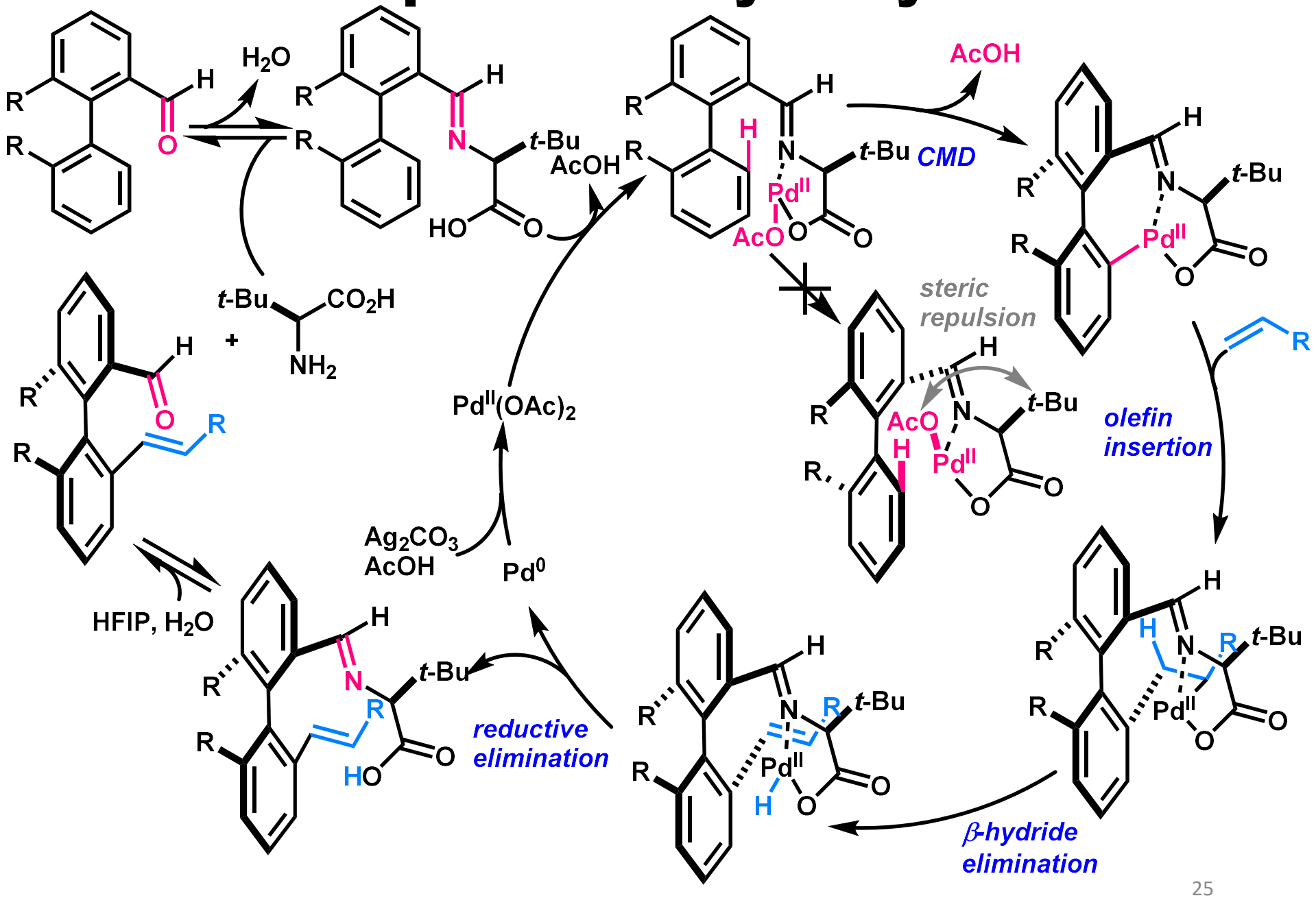
Installation of Axial Chirality



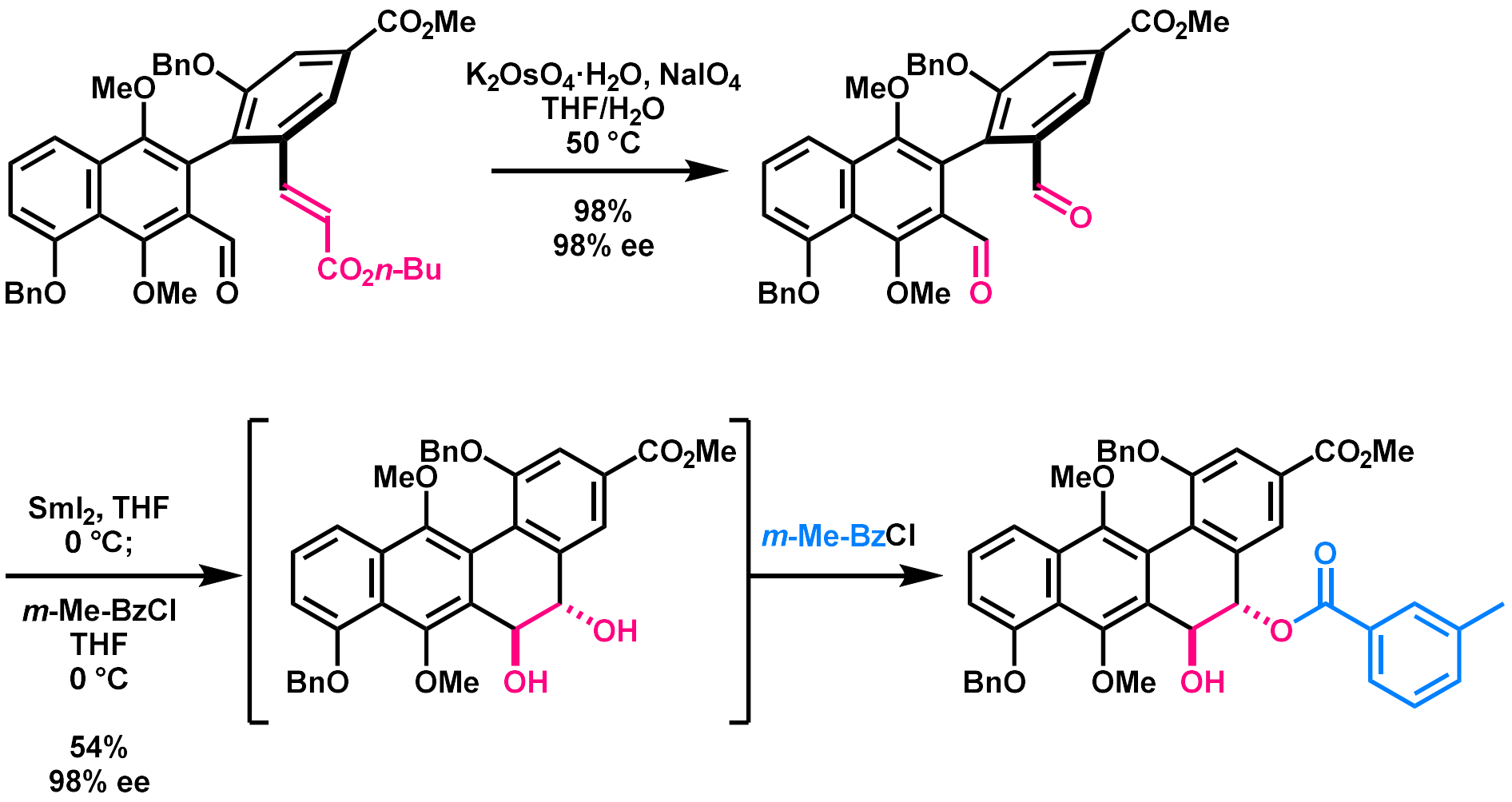
1) Fan, J.; Yao, Q.-J.; Liu, Y.-H.; Liao, G.; Zhang, S.; Shi, B.-F. *Org. Lett.* **2019**, *21,* 3352.

Proposed Catalytic Cycle



1) Yao, Q.-J.; Zhang, S.; Zhan, B.-B.; Shi, B.-F. *Angew. Chem. Int. Ed* **2017**, *56,* 6617.

Pinacol Coupling



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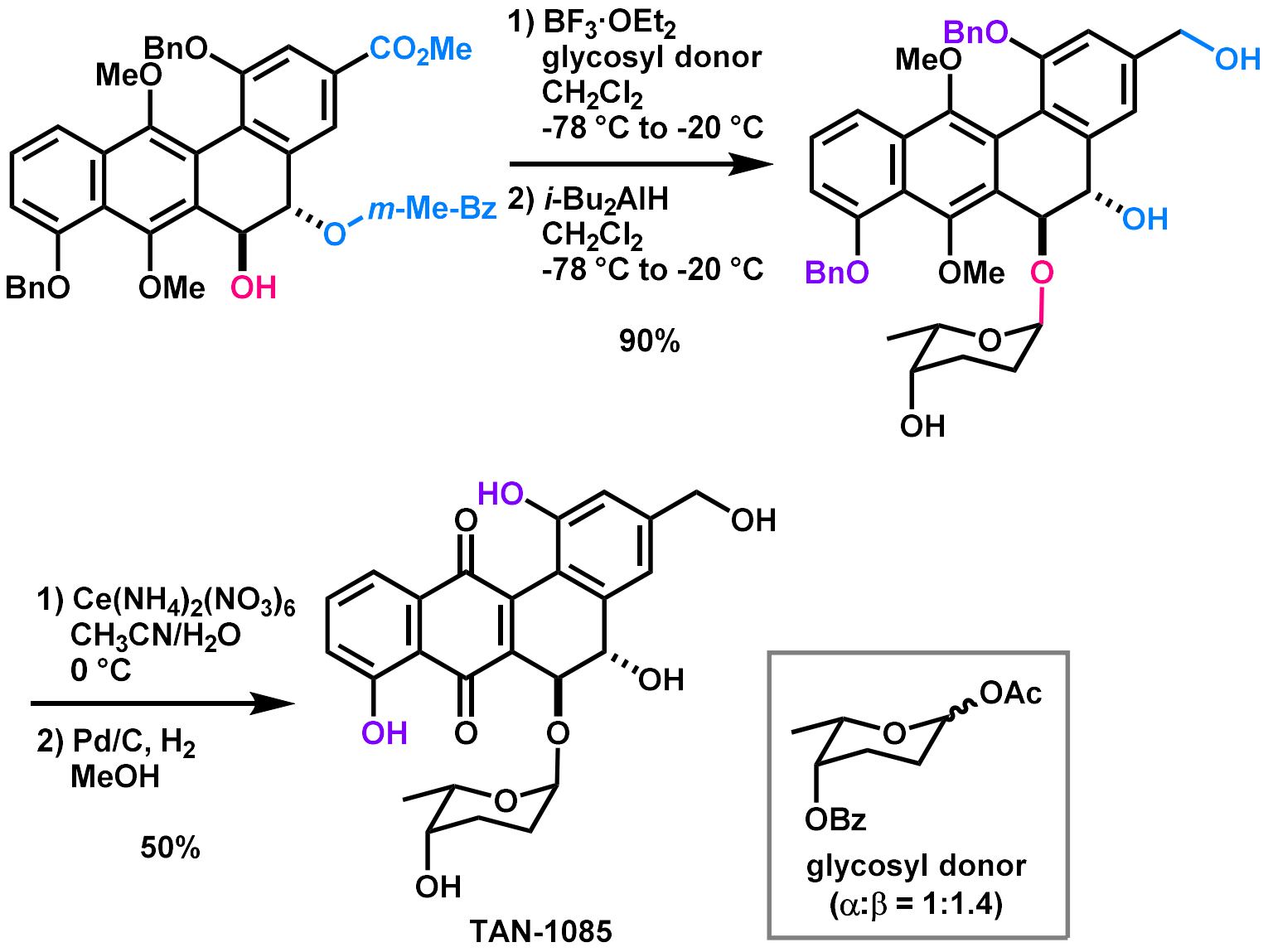
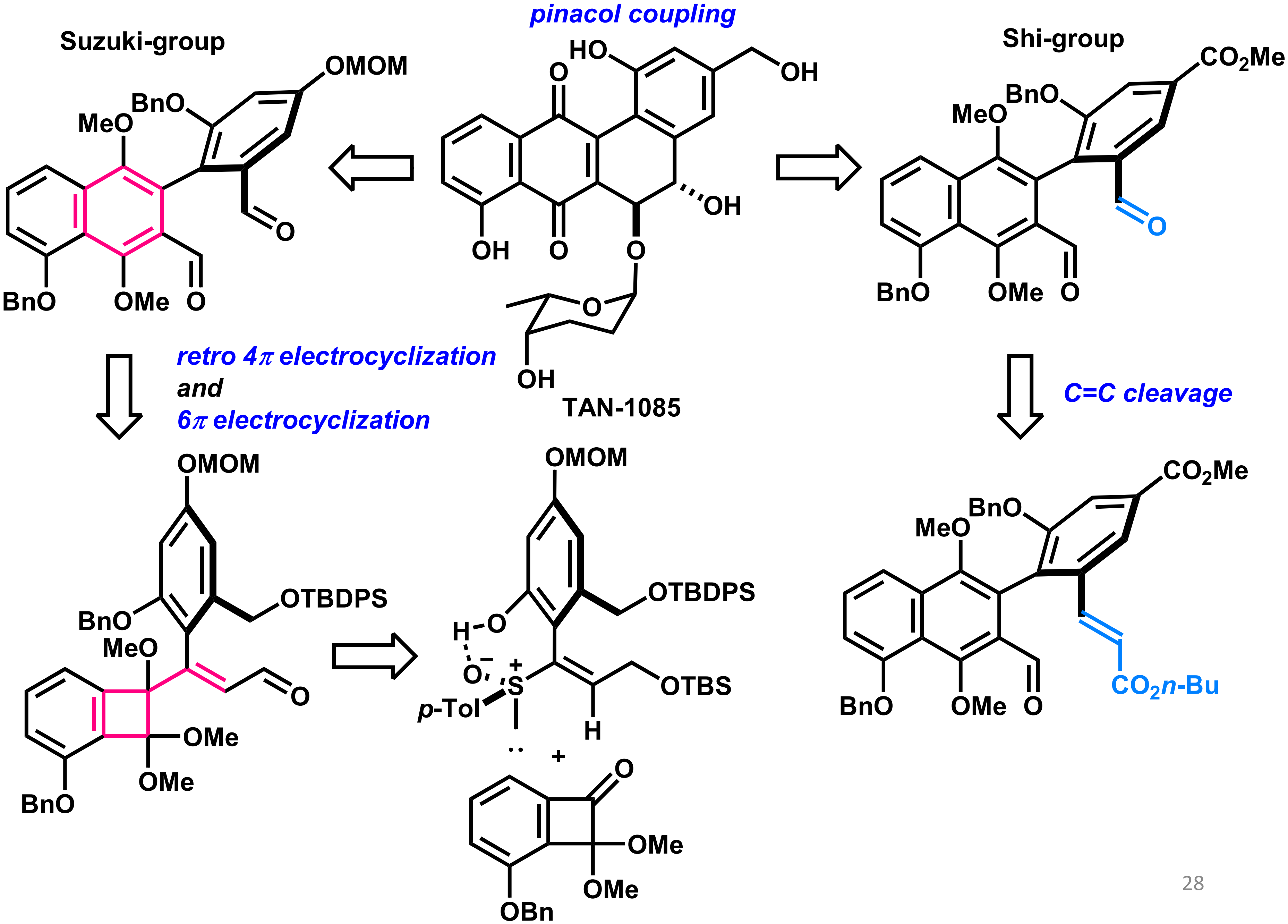
Total Synthesis of TAN-1085



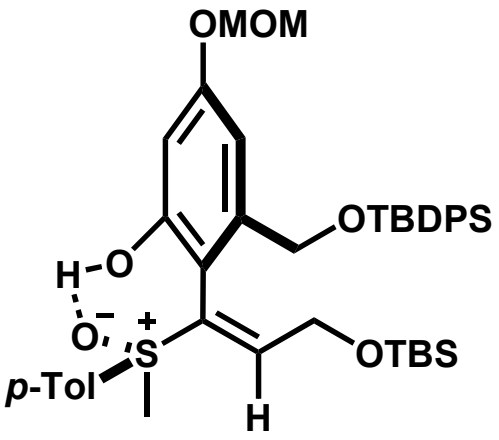
1) Fan, J.; Yao, Q.-J.; Liu, Y.-H.; Liao, G.; Zhang, S.; Shi, B.-F. *Org. Lett.* **2019**, *21,* 3352.

Summary

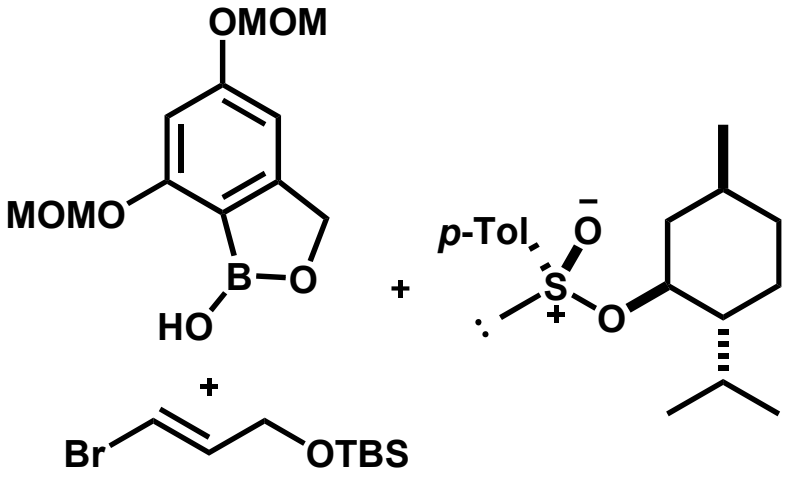

pinacol coupling
Suzuki-group
Shi-group
TAN-1085
retro 4π electrocyclization
and
6π electrocyclization
C=C cleavage
OMOM
BnO
MeO
OMe
O
HO
OH
CO2Me
OTBDPS
OTBS
H-O
p-Tol
S
H
OBn
CO2n-Bu

Summary

Suzuki-group



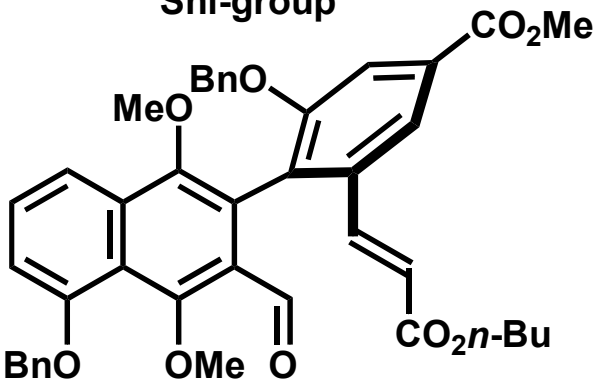
Suzuki-Miyaura coupling



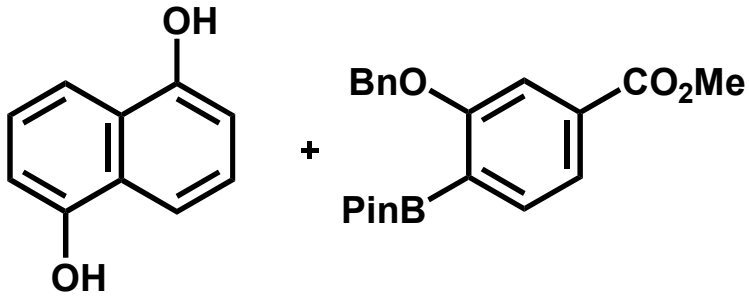
21 steps from vinyl bromide
5% yield

- Chiral biaryl can be synthesized by only intramolecular interaction.
- First total synthesis using chiral relay strategy

Shi-group



asymmetric C-H olefination
and
Suzuki-Miyaura coupling



16 steps from dihydroxynaphthalene
3% yield

- Only catalytic amount of reagents are needed to make chirality.
- C-H activation is used in total synthesis