JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
1999

# Literature Talk, Birte Schröder, 05.03.15, AK Gaich Group Seminar

# Some Fact about JACS1999

- Published articles: 2,166
- Pages: 12216
- Articles with „Total Synthesis“: 244

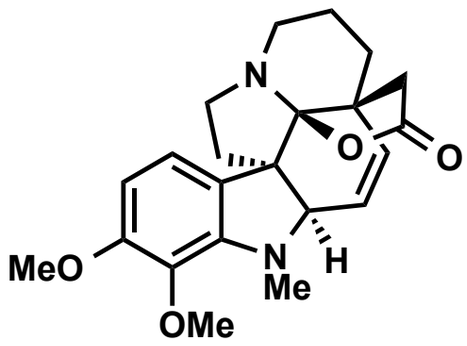
**Most profilic authors:**

- Trost, B. M. (16)
- Houk, K. N. (16)
- Buchwald, S. L. (11)
- Solomon, E. I. (10)
- Whitesides, G. M. (10)
- Rebek, J. (9)
- Adam, W. (9)
- Schuster, G. B. (8)
- Boger, D. L. (8)
- Danishefsky, S. J. (8)

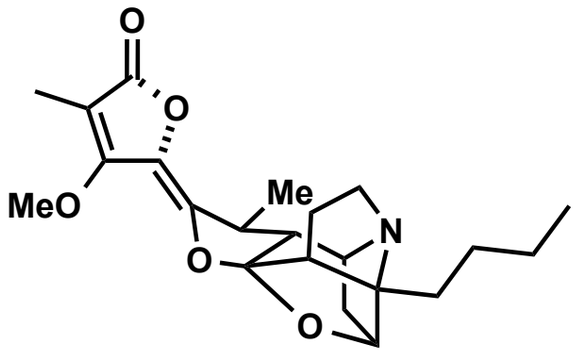
**Contribution by countries:**

- USA (1,355)
- Japan (250)
- Germany (144)
- United Kingdom (119)
- Canada (102)

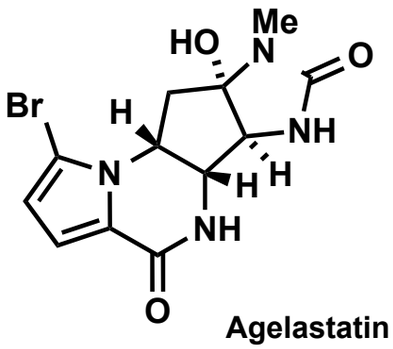
# Detailed Synthesis



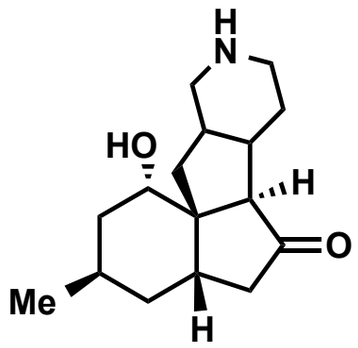

**Aspidophytine**



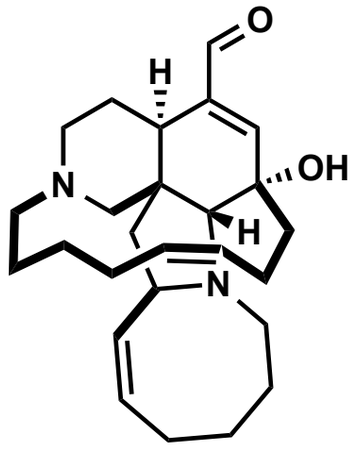

**Isostemofoline**



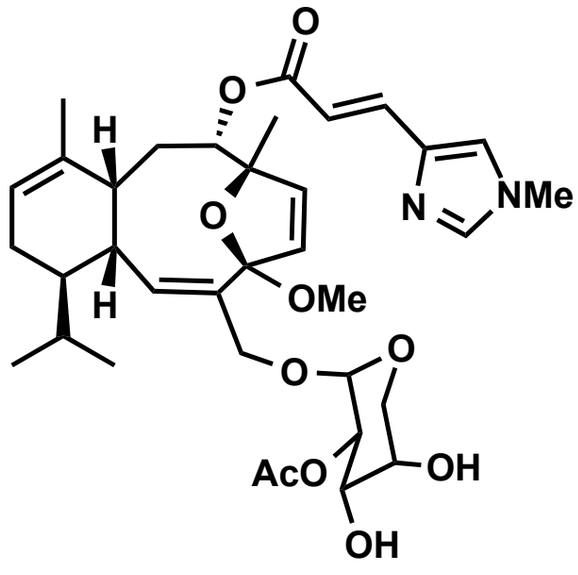

**Agelastatin**




**Paniculatine**

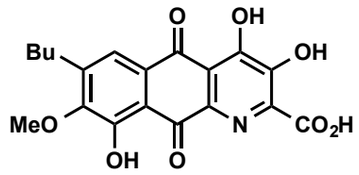



**Ircinal A**



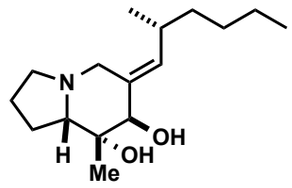

**Eleutherobin**

# Key steps



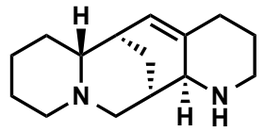

**Phomazarin**

hetero Diels-Alder




**Allopumikiotoxin**

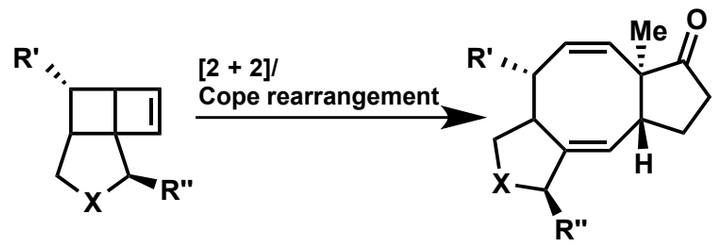
Ni-cat. reductive cyclization

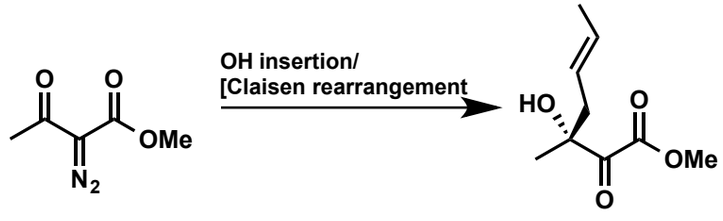



**Aloperine**

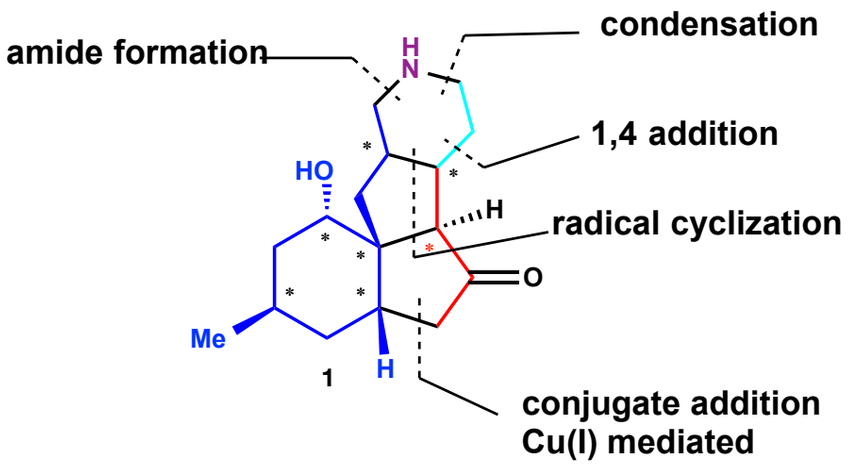
Intramolecular Diels-Alder

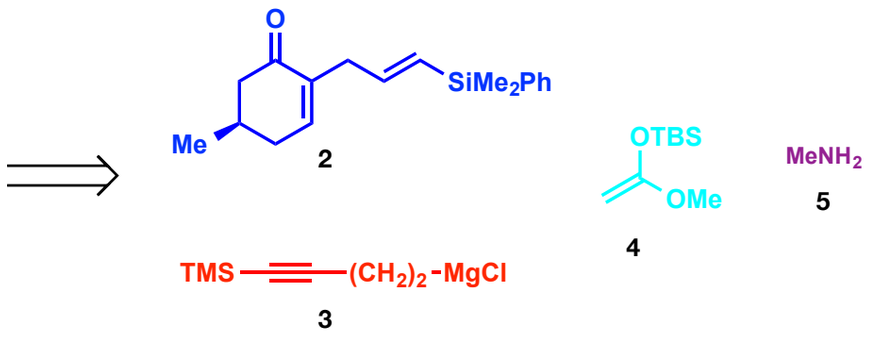
# Methodologies



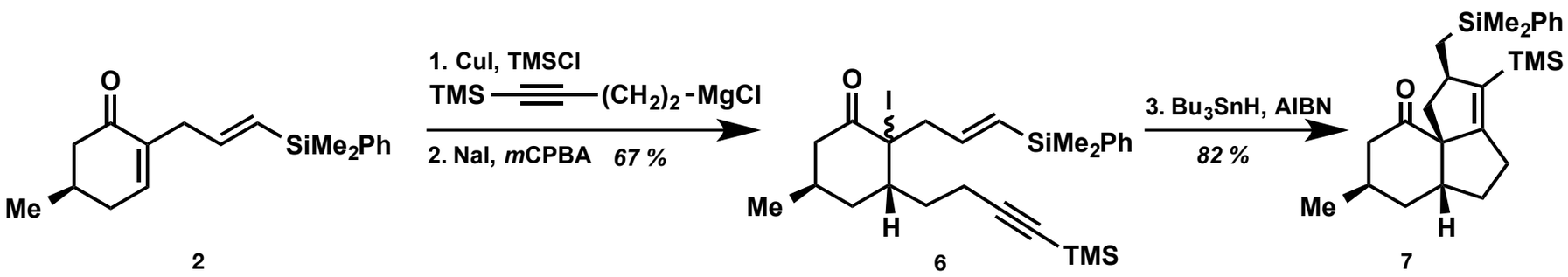
# Sha Group: (+)-Paniculatine




- Structural Features:
  - Tetracyclic skeleton with an angularly fused tricyclic ketone
  - 7 stereocenters:
    - 5 of them are consecutive
    - 1 quaternary stereocenter
- Key step: radical cyclization

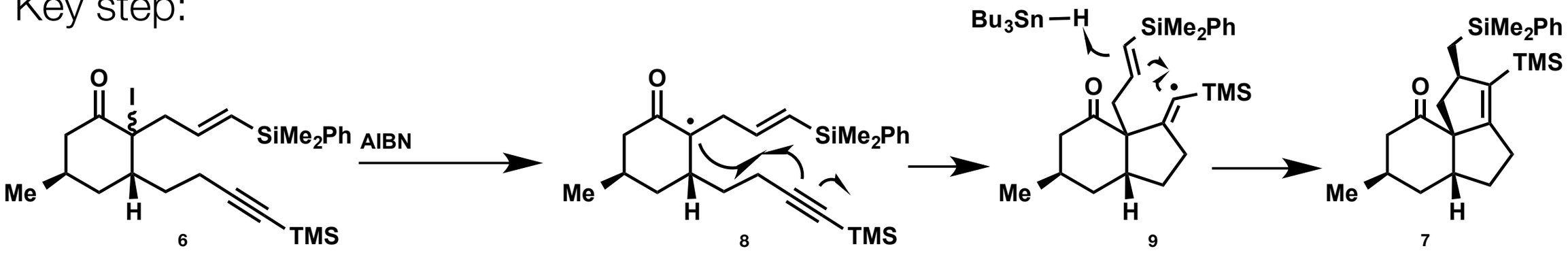
*J. Am. Chem. Soc*. **1999**, *121*, 866-867.

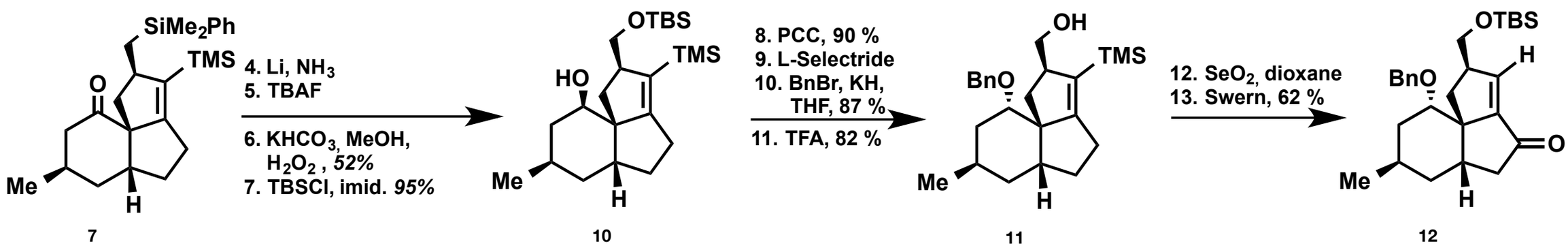



*Tetrahedron Lett*. **1995**, *36*, 351.

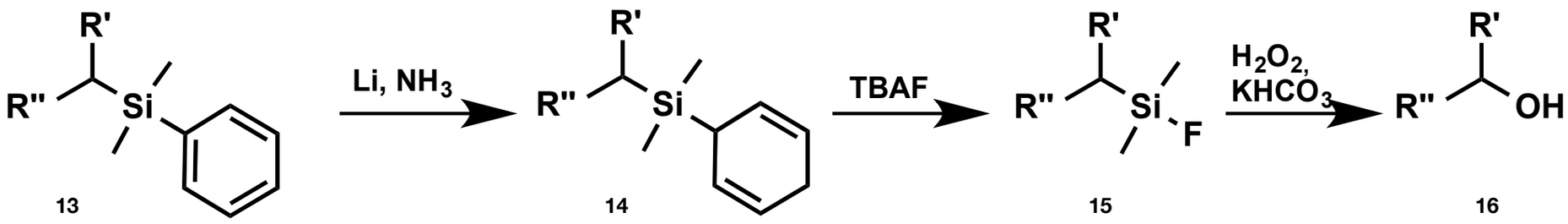
# Sha Group: (+)-Paniculatine

Key step:



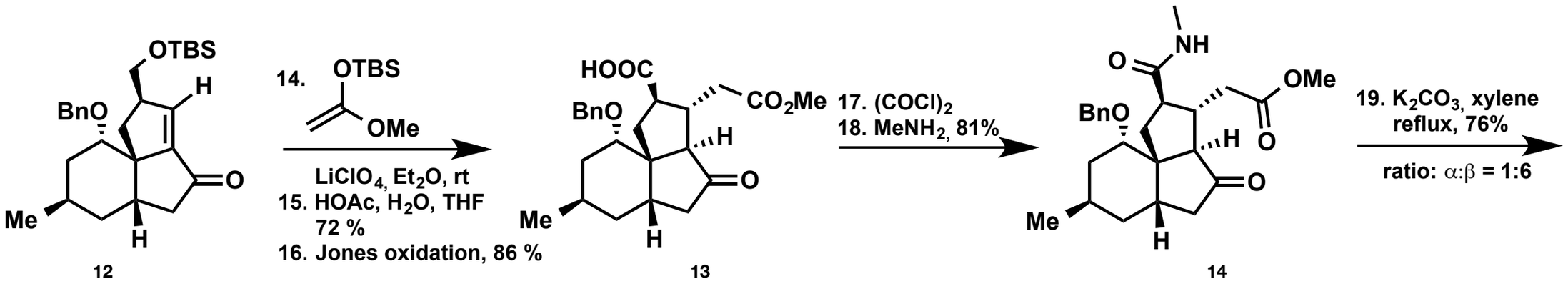



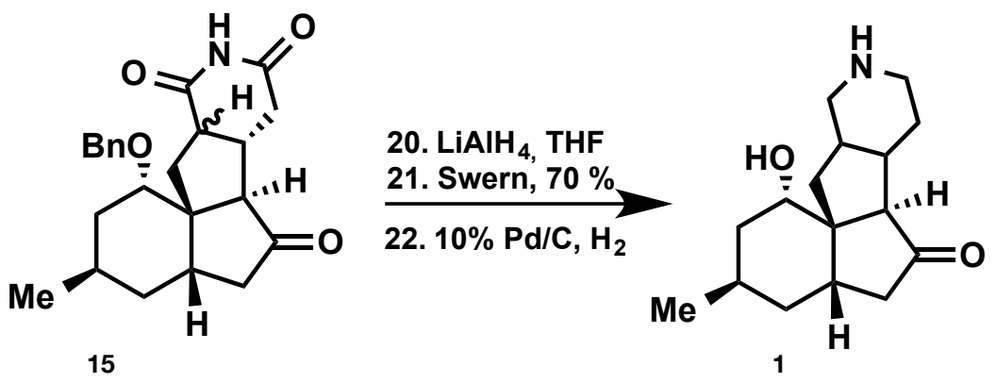

Taber's methodology:



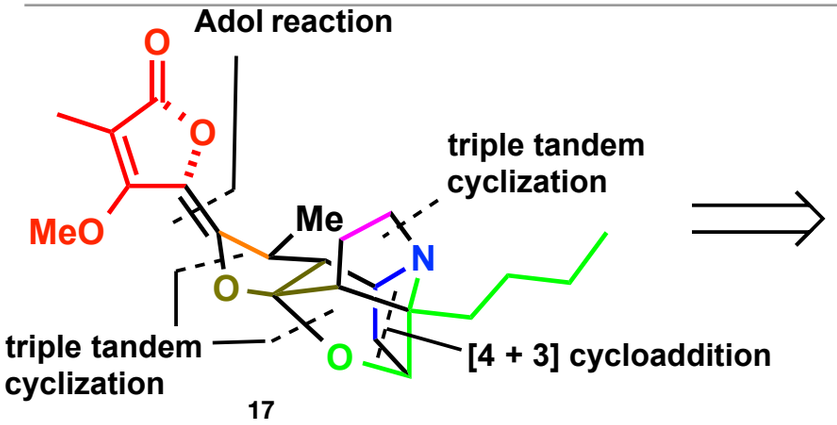

- Tamao-Flemming oxidation: activation of the phenyl group with e. g. KBr, $BF_3 * 2AcOH$, $HBF_4 * OEt_2$

# Sha Group: (+)-Paniculatine

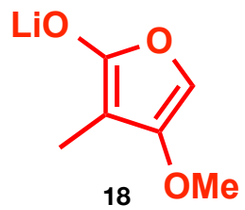


# Kende Group: (+) Isostemofoline




Isostemofoline

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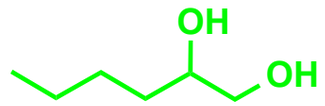


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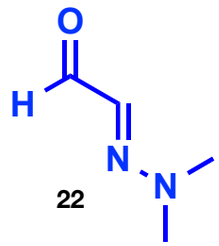


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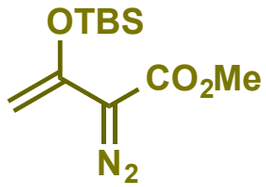


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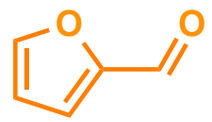


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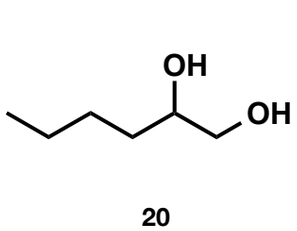
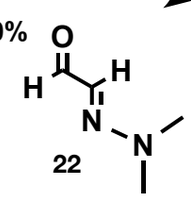
- Structural Features:
  - Pentacyclic core with a pendant conjugated butenolide
- Key Steps:
  - triple tandem cyclization
  - [4+3] cycloaddition

*J. Am. Chem. Soc*. **1999**, *121*,7431-32.




20

1. 13% aq. NaOCl, HOAc, 65 %
2. MOMCl, DiPEA, 93%
3. KOEt, 80%

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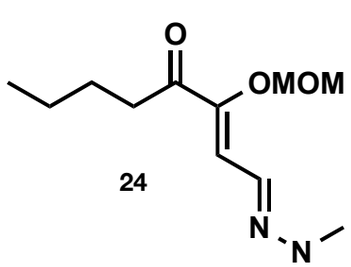


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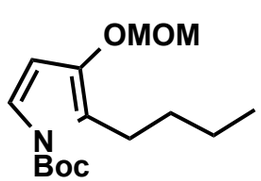
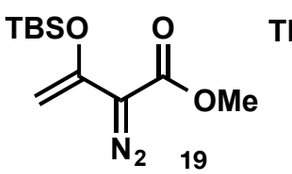
4. $Na_2S_2O_4$, EtOH, $H_2O$, 90°C, 35%
5. $Boc_2O$, DMAP, MeCN, 72%

reductive cyclization




25

6. Rhodium octanoate dimer, pentane, reflux, 90%

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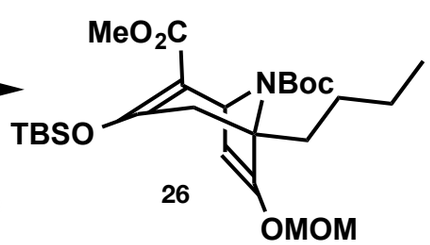


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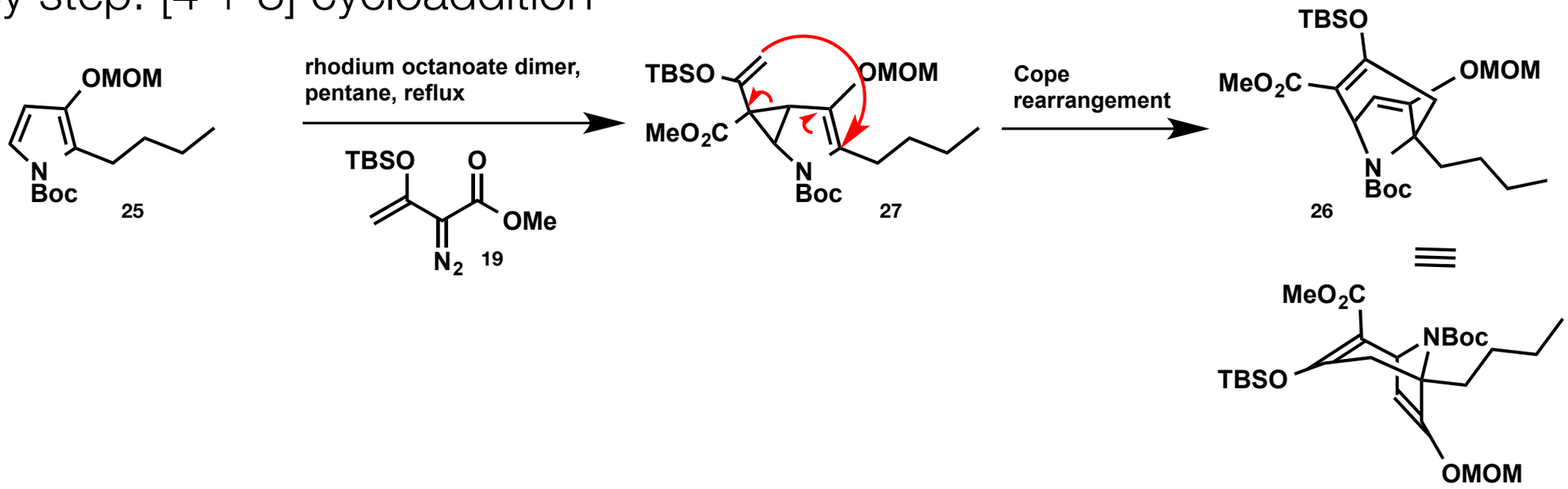
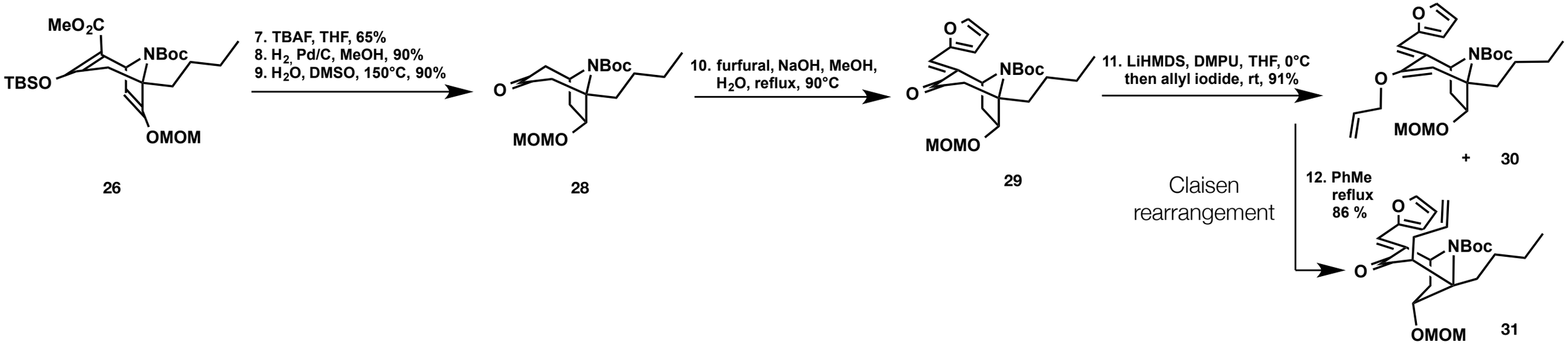
[4+3] cycloaddition

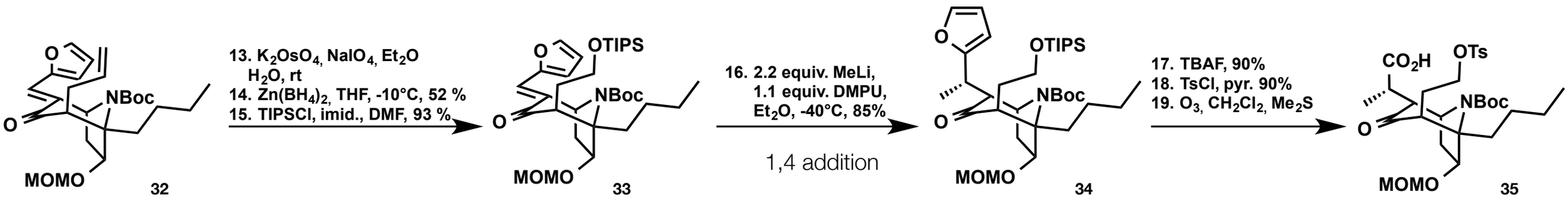
# Kende Group: (+) Isostemofoline

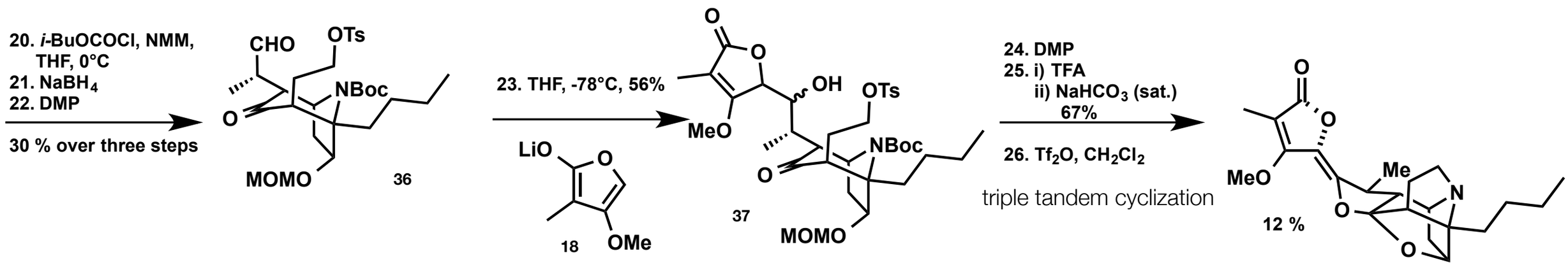
## Key step: [4 + 3] cycloaddition



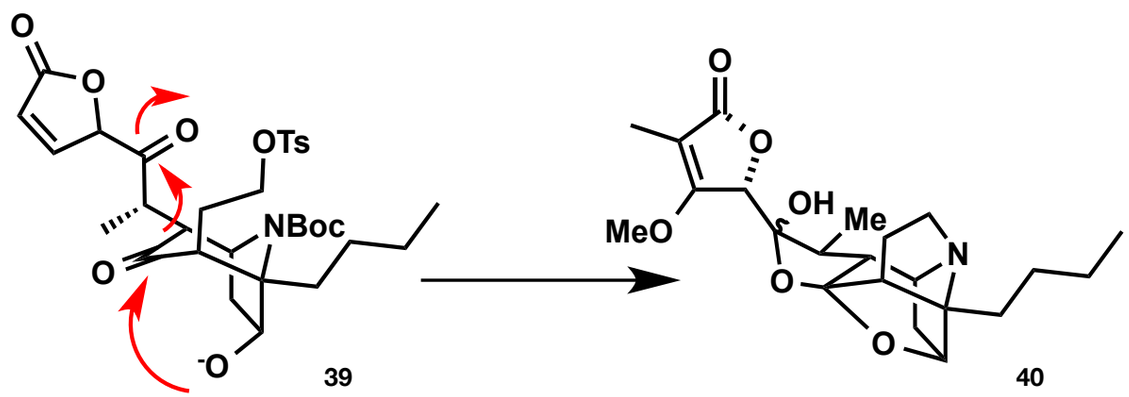



# Kende Group: (+) Isostemofoline

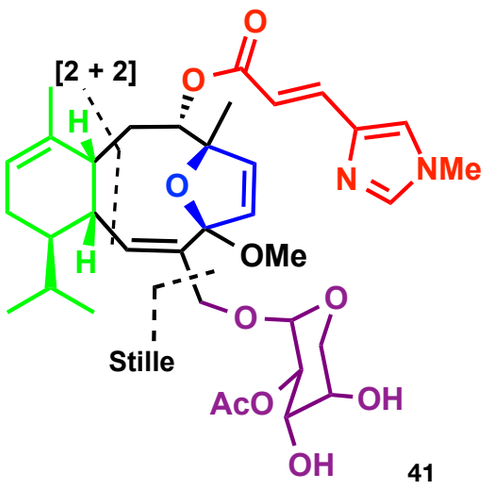



Key step: triple tandem cyclization



# Danishefsky Group: Eleutherobin

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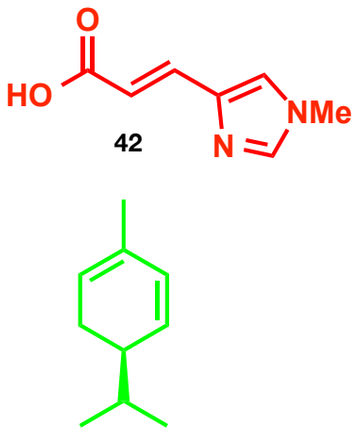


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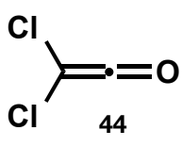


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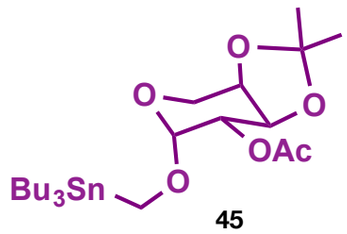


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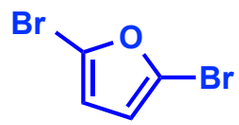


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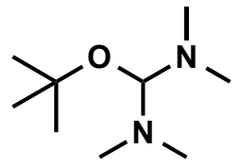


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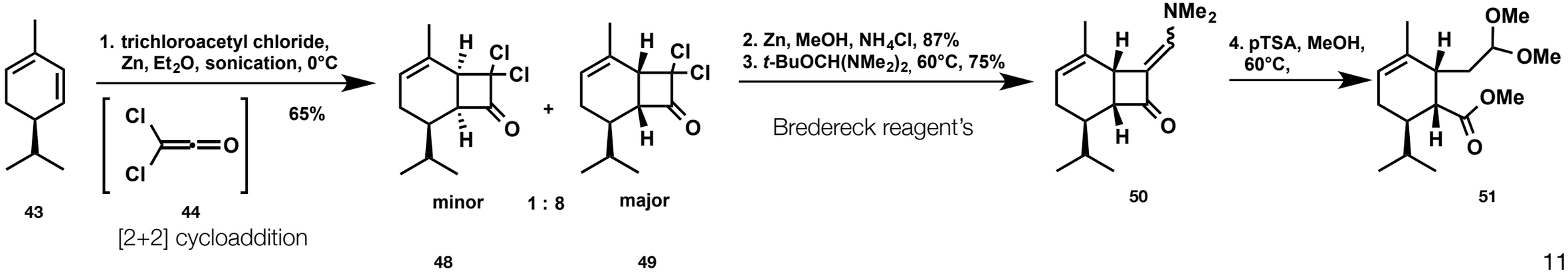
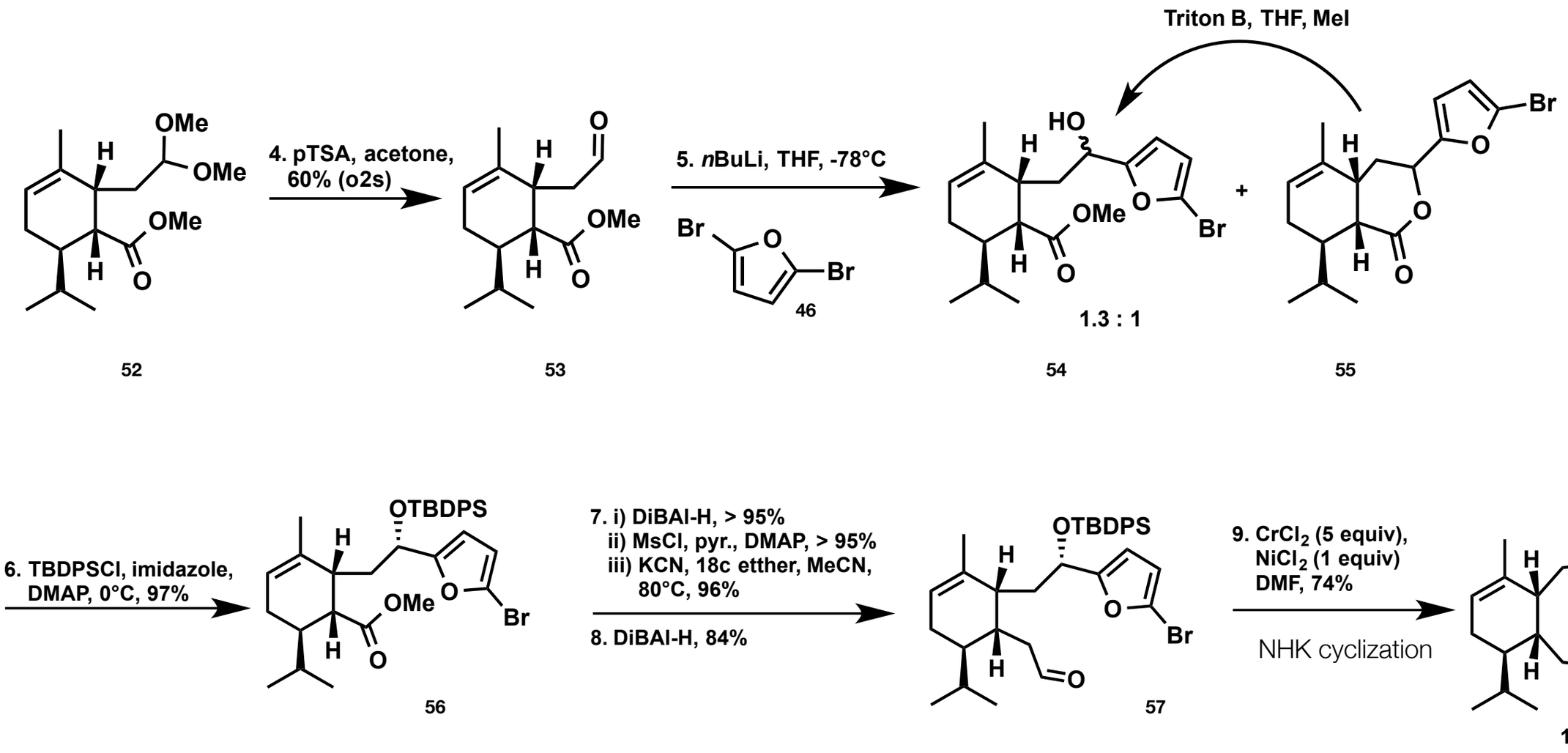
- Structural Features:
  - 10 stereogenic centers
  - urocanic ester linkage
  - arabinose domain
  - aglycon sector
- Key Steps:
  - NHK ring closure
  - transposition of a pyranose to a furanose
  - novel oxacarbyglycosidation

*J. Am. Chem. Soc*. **1999**, *121*, 6563-6579.

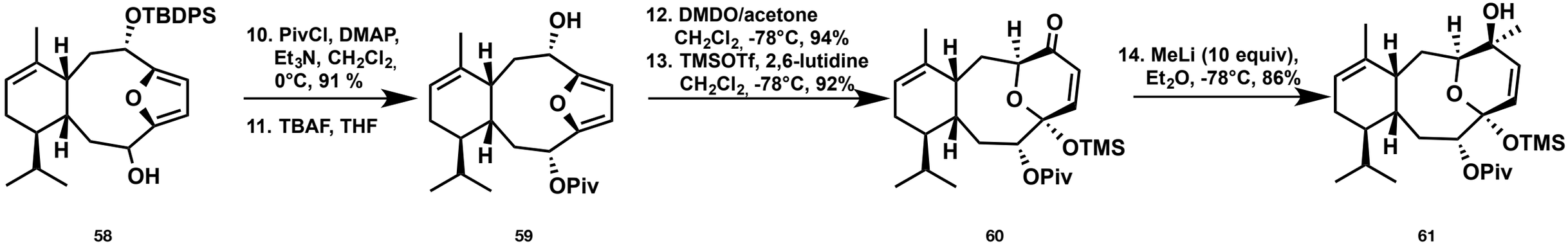



43 44 [2+2] cycloaddition 48 49 50 51

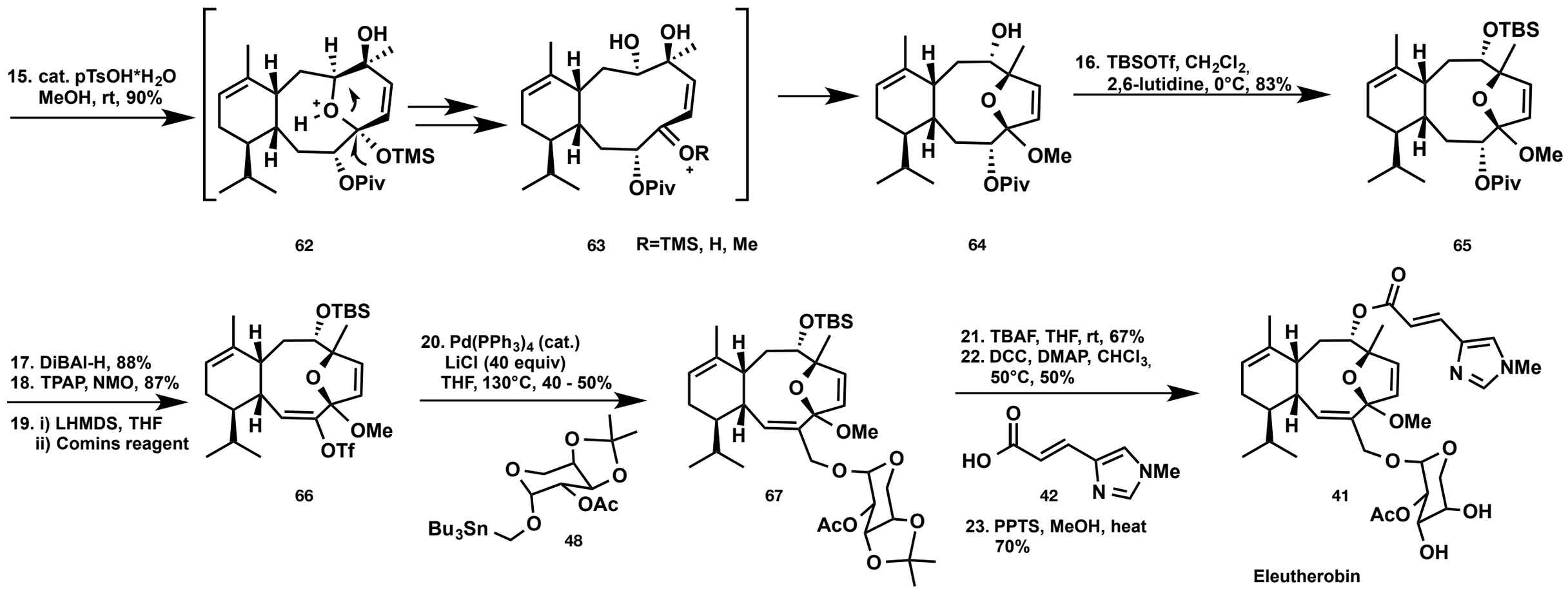
# Danishefsky Group: Eleutherobin



# Danishefsky Group: Eleutherobin




58 59 60 61

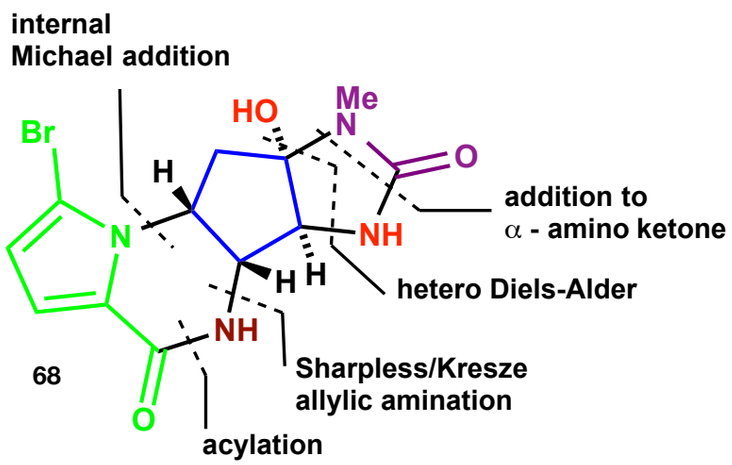


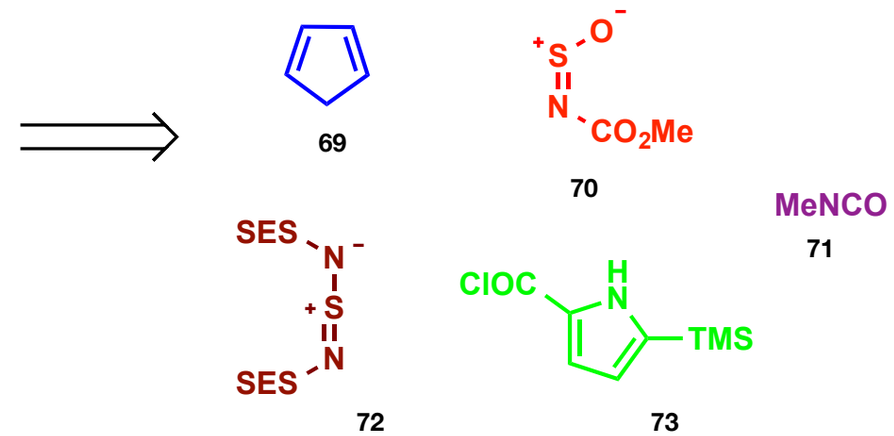

62 63 R=TMS, H, Me 64 65

66 48 67 42 41

Eleutherobin

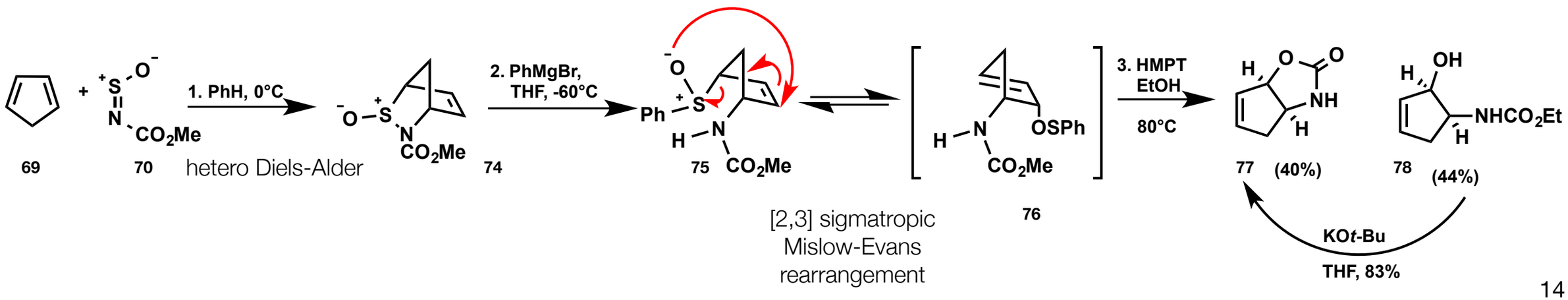
# Weinreb Group: Agelastatin A



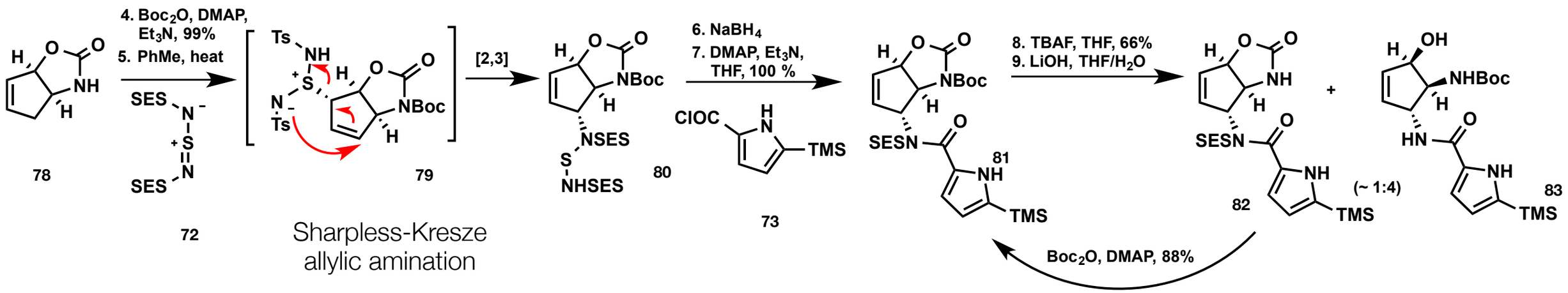



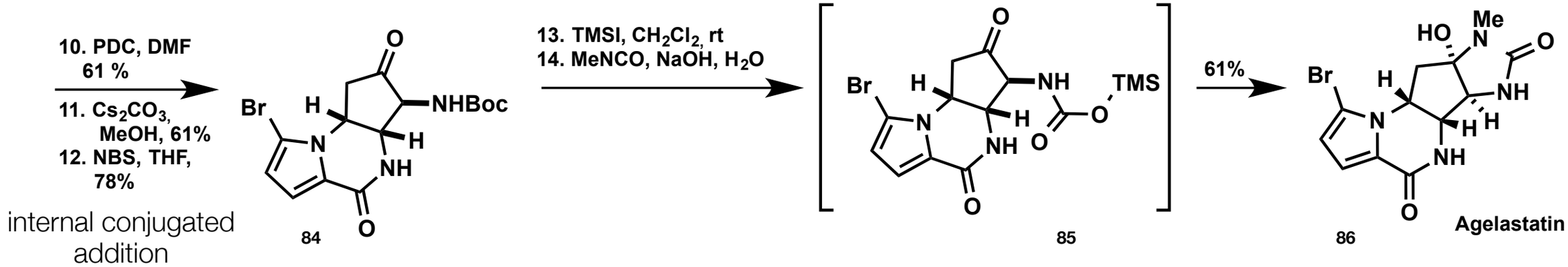

- Structural Features:
  - Tetracyclic alkaloid with four stereogenic centers
- Key steps:
  - hetero Diels-Alder reaction
  - Sharpless/Kresze allylic amination with a sulfodiimide

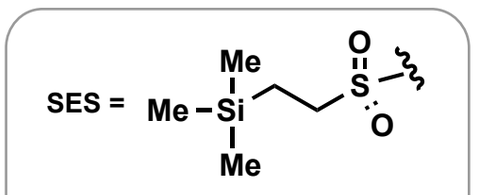
*J. Am. Chem. Soc.* **1999**, *121*, 9574-9579.



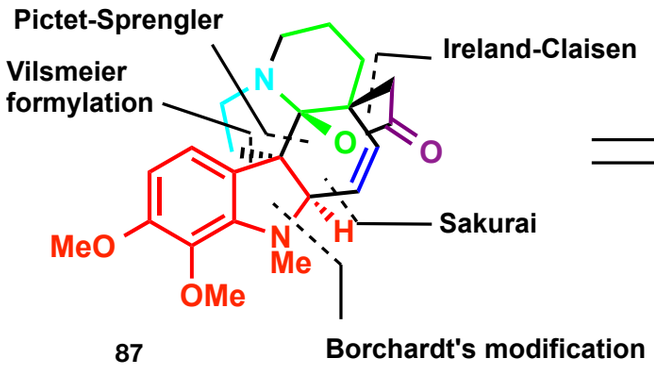
# Weinreb Group: Agelastatin A

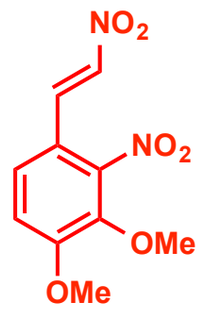


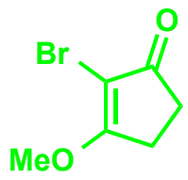



# Corey Group: Aspidophytine

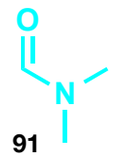


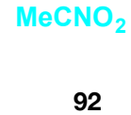



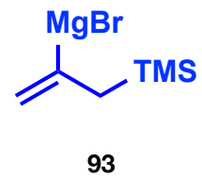



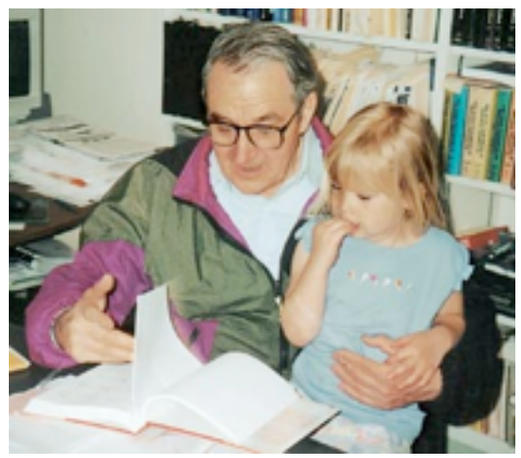






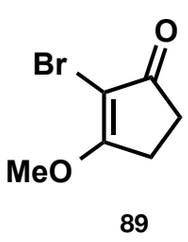



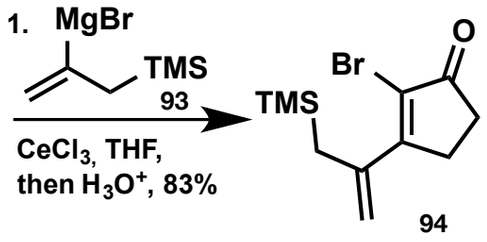



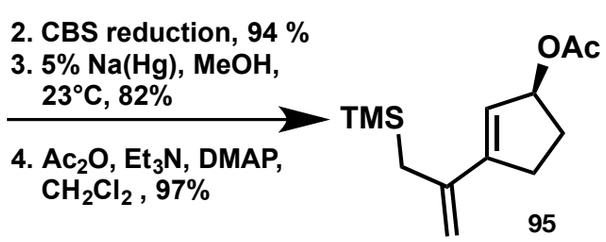



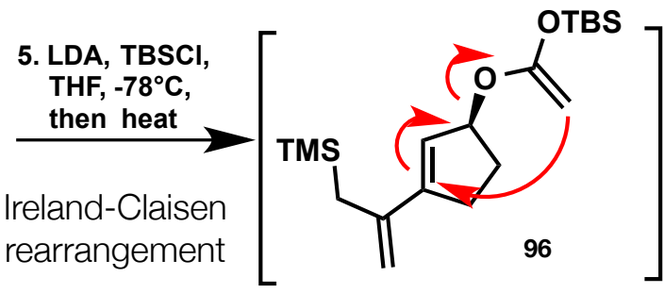
- Indole Alkaloid containing 4 stereogenic centers
  - two quaternary carbon centers

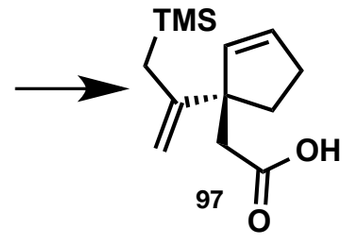
*J. Am. Chem. Soc.* **1999**, *121*, 6771-6772.

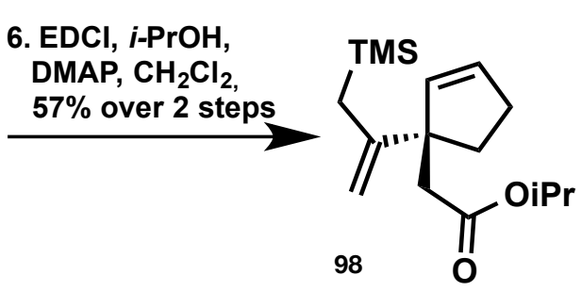


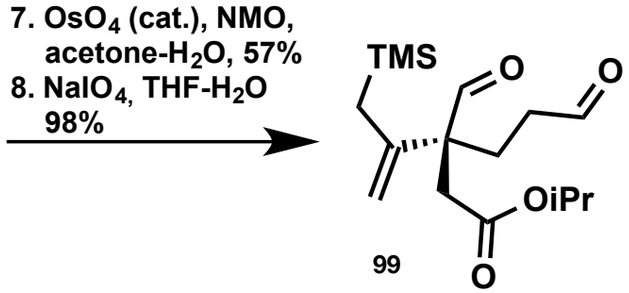



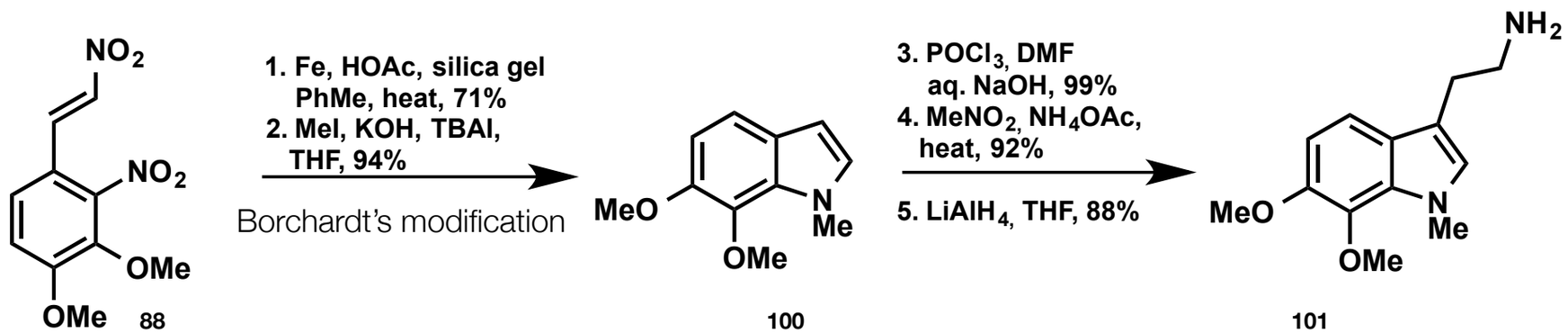



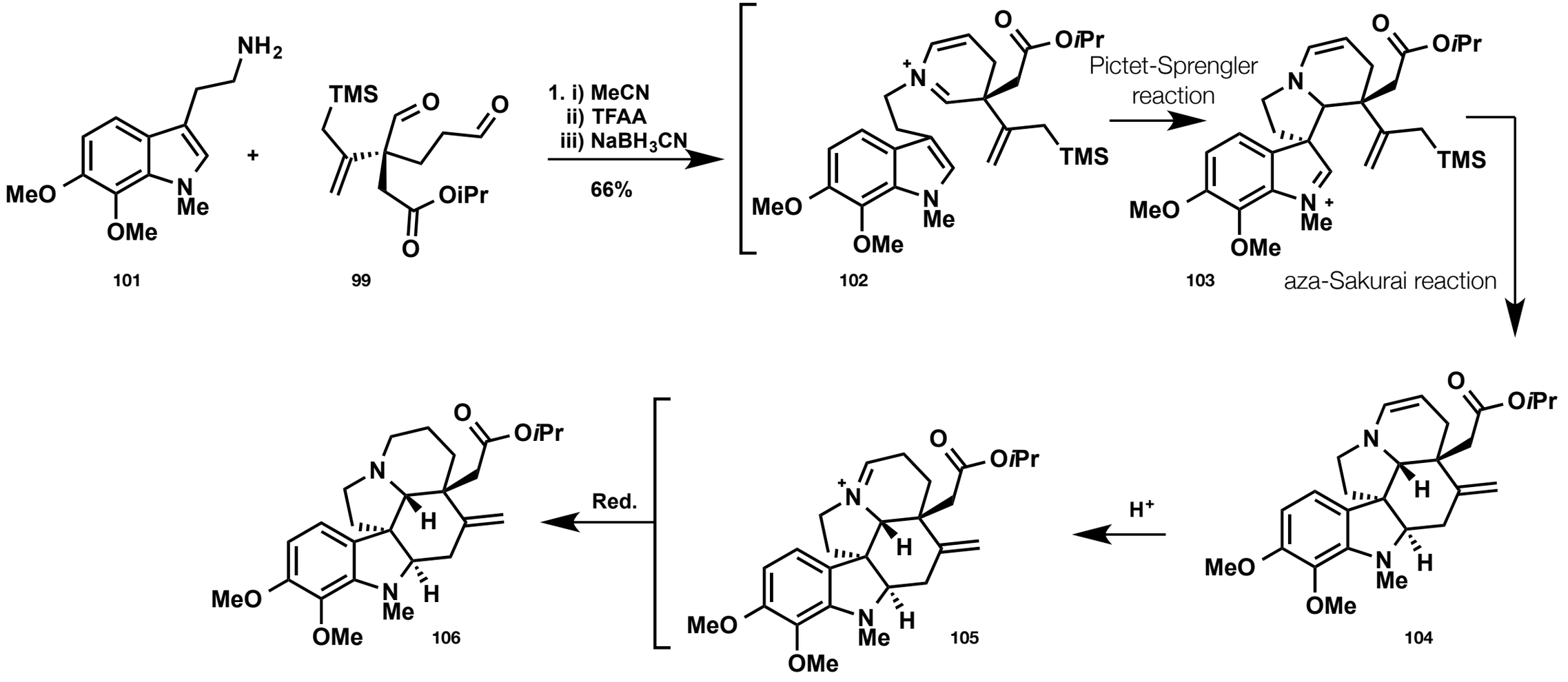



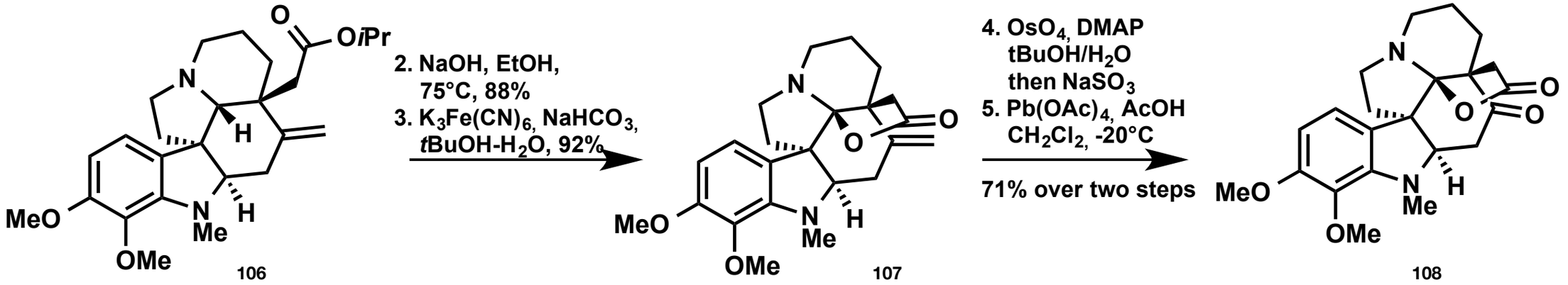



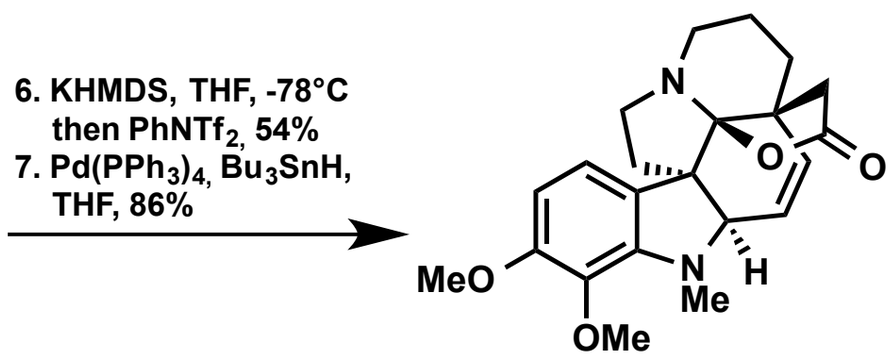
# Corey Group: Aspidophytine



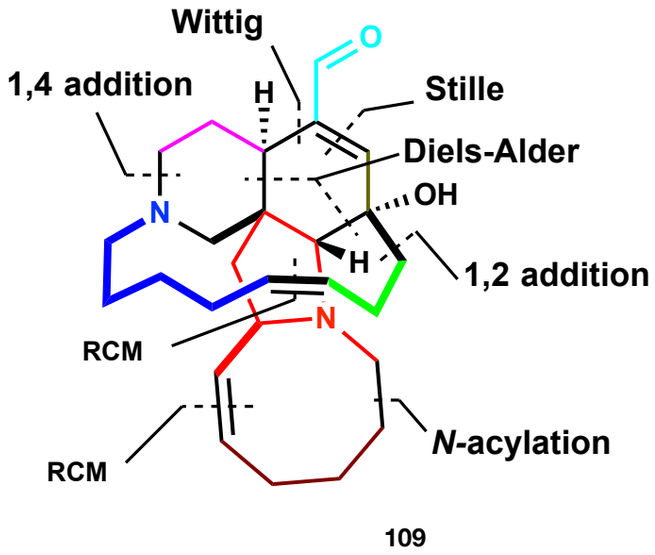



# Corey Group: Aspidophytine

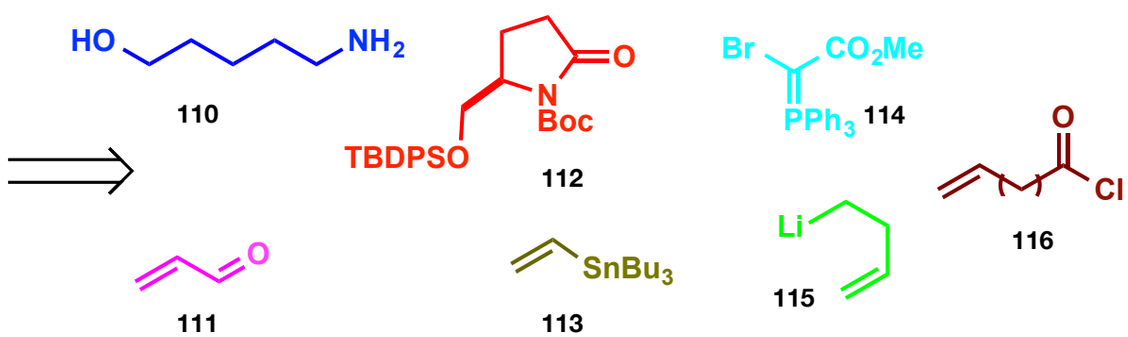


# Martin Group: Ircinal A

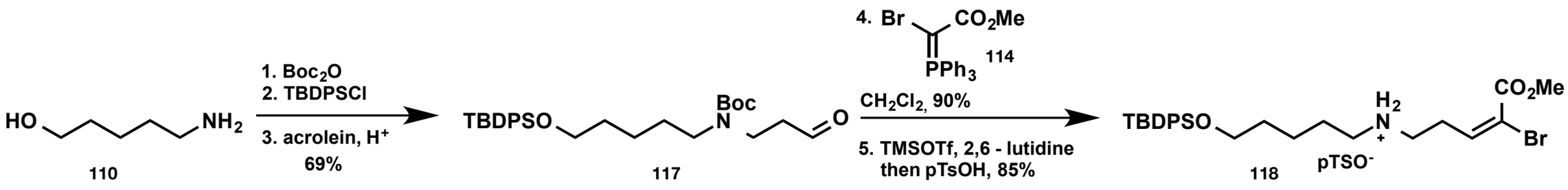



109



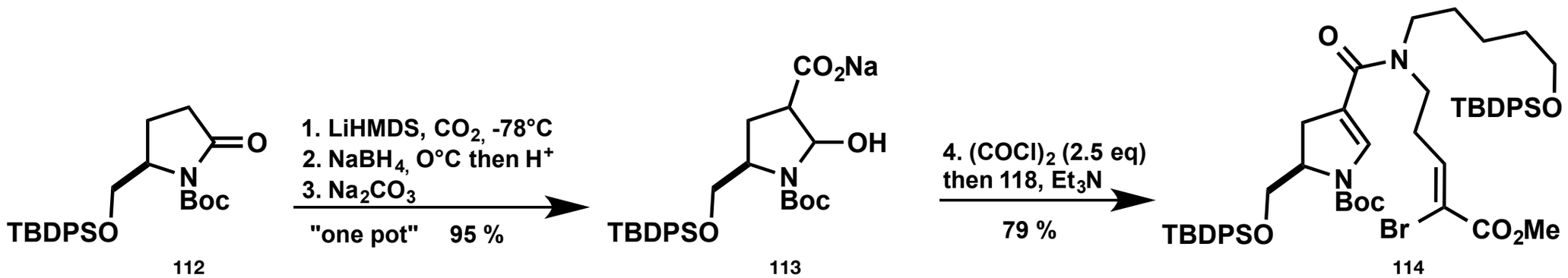

- Related to the Manzamine indol alkaloids
- Structural features:
  - 8-membered ring
  - 13-membered ring
  - tricyclic (6-6-5) core structure
- Key steps: domino-Stille/Diels-Alder reaction
  RCM reactions

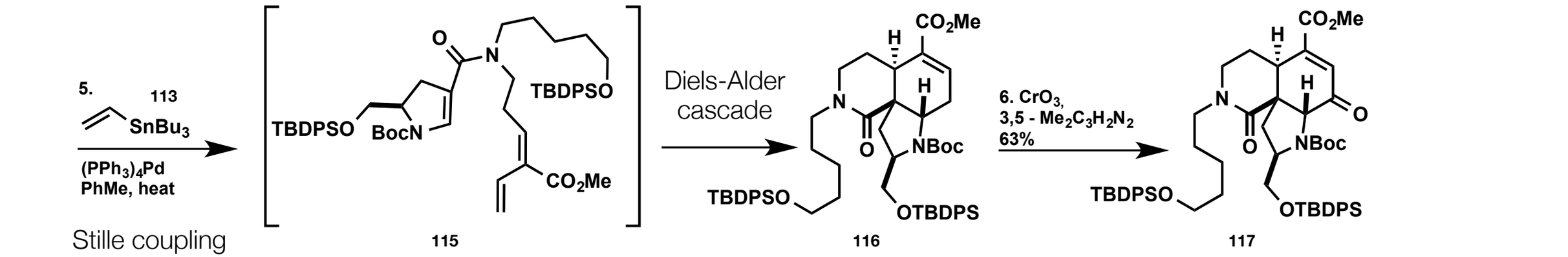
*J. Am. Chem. Soc.* **1999**, *121*, 866-867.

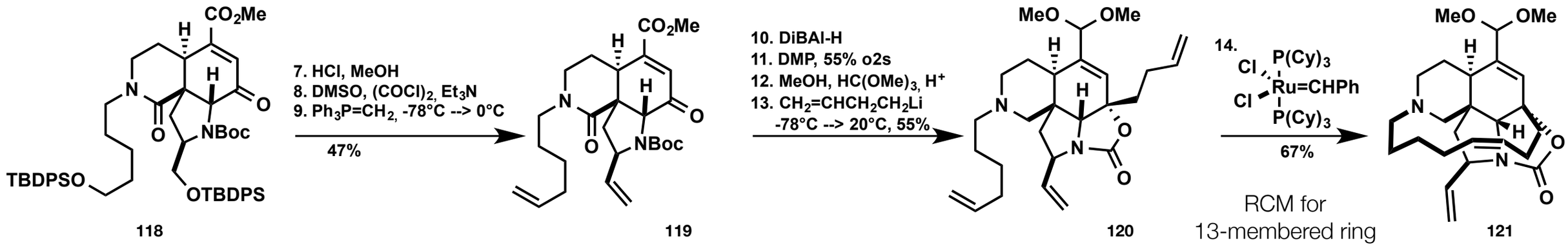



1,4 - addition

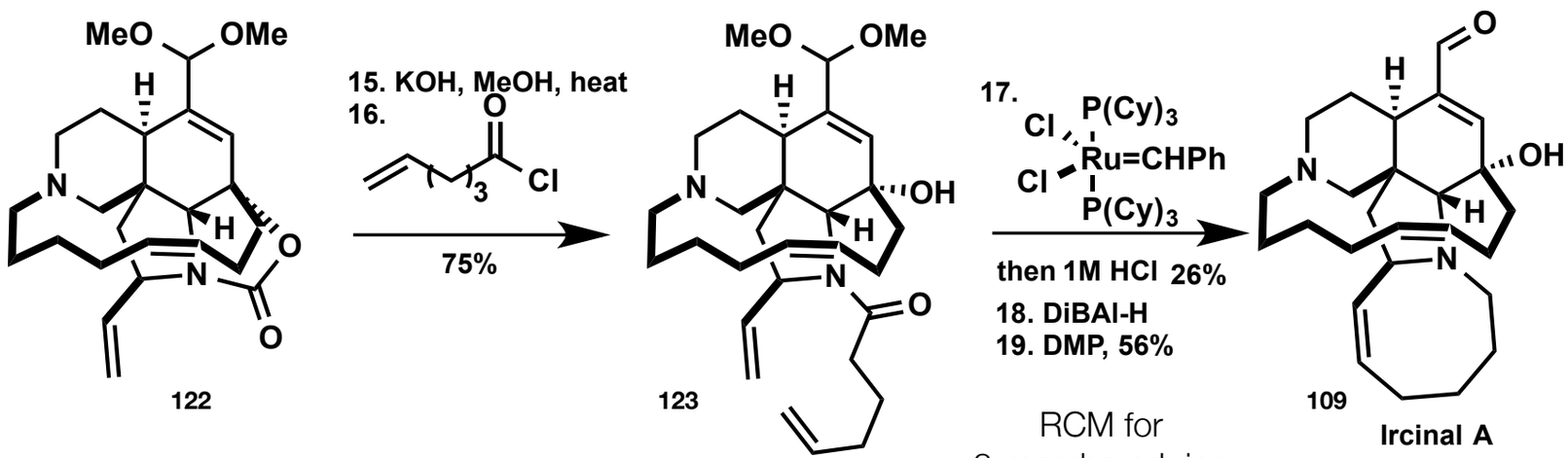
# Martin Group: Ircinal A



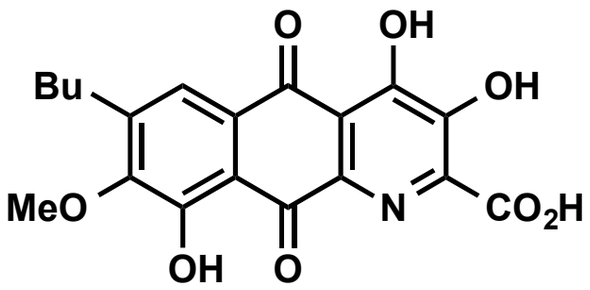



# Martin Group: Ircinal A

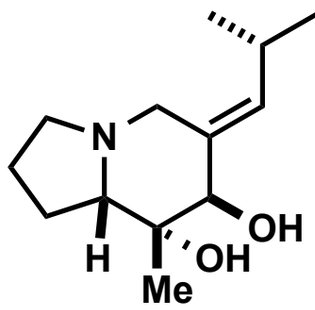


# Key steps in Total Synthesis

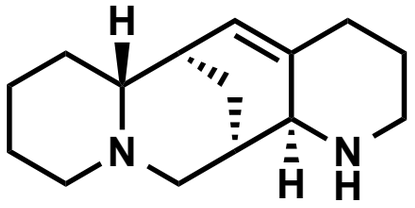
JACS 1999




Phomazarin

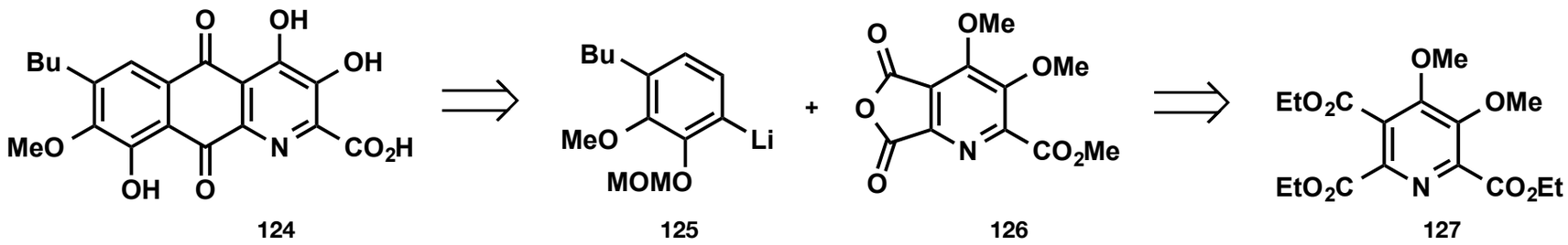



Allopumikiotoxin



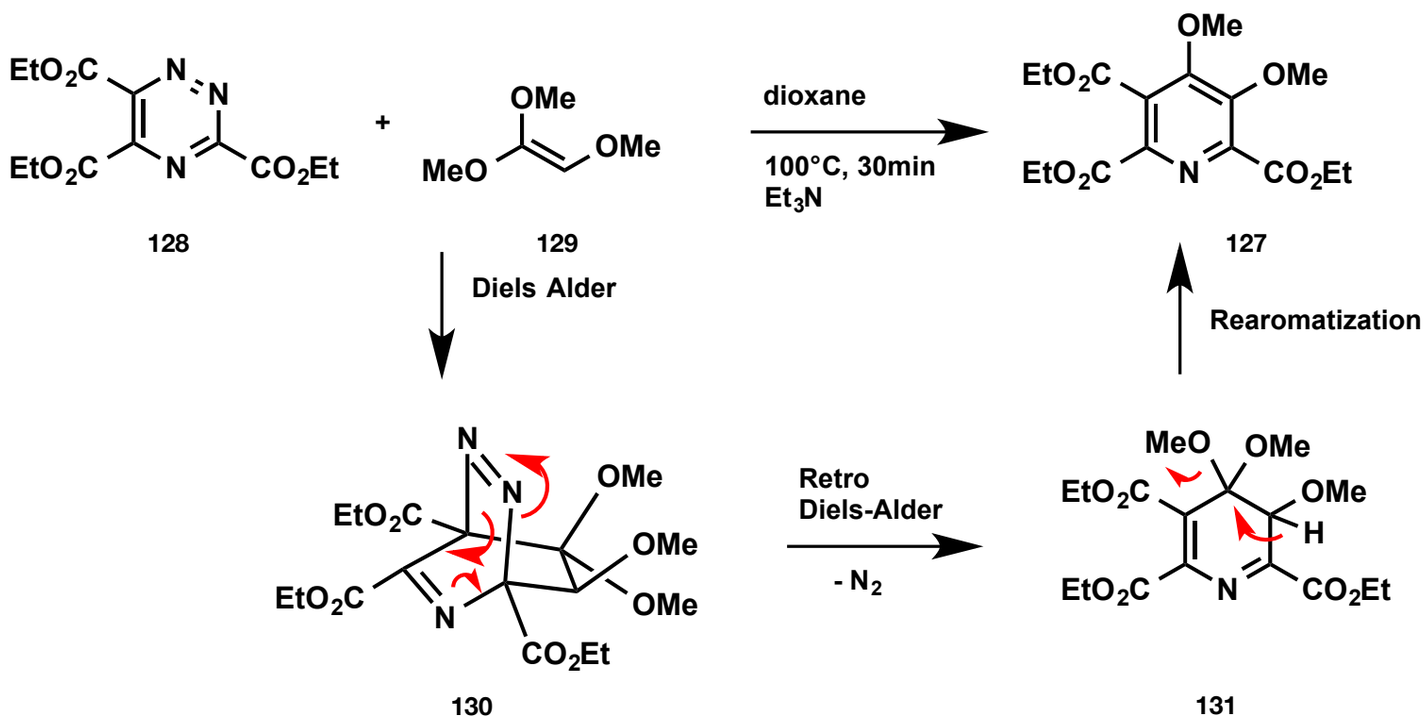

Aloperine

# Boger Group: Phormazarin



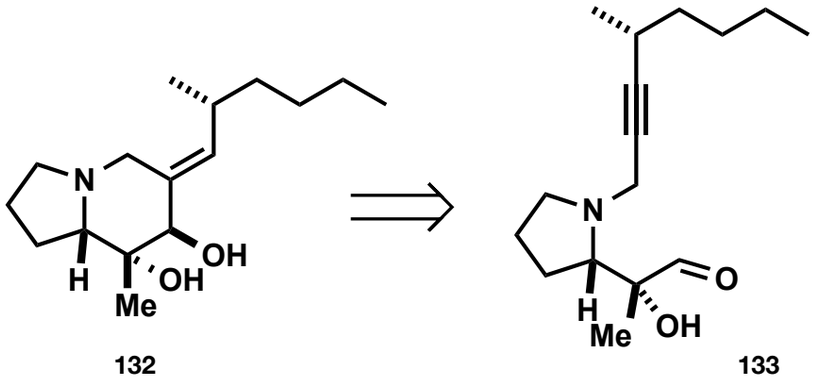

- <u>Key step:</u>
  Pyridine synthesis *via* an heteroaromatic azadiene Diels-Alder reaction

*J. Am. Chem. Soc.* **1999**, *121, 2471-2477*.




- Inverse electronic demand:
  - electron-deficient 1,2,4-triazine
  - electron-rich 1,1,2-trimethoxyethylene

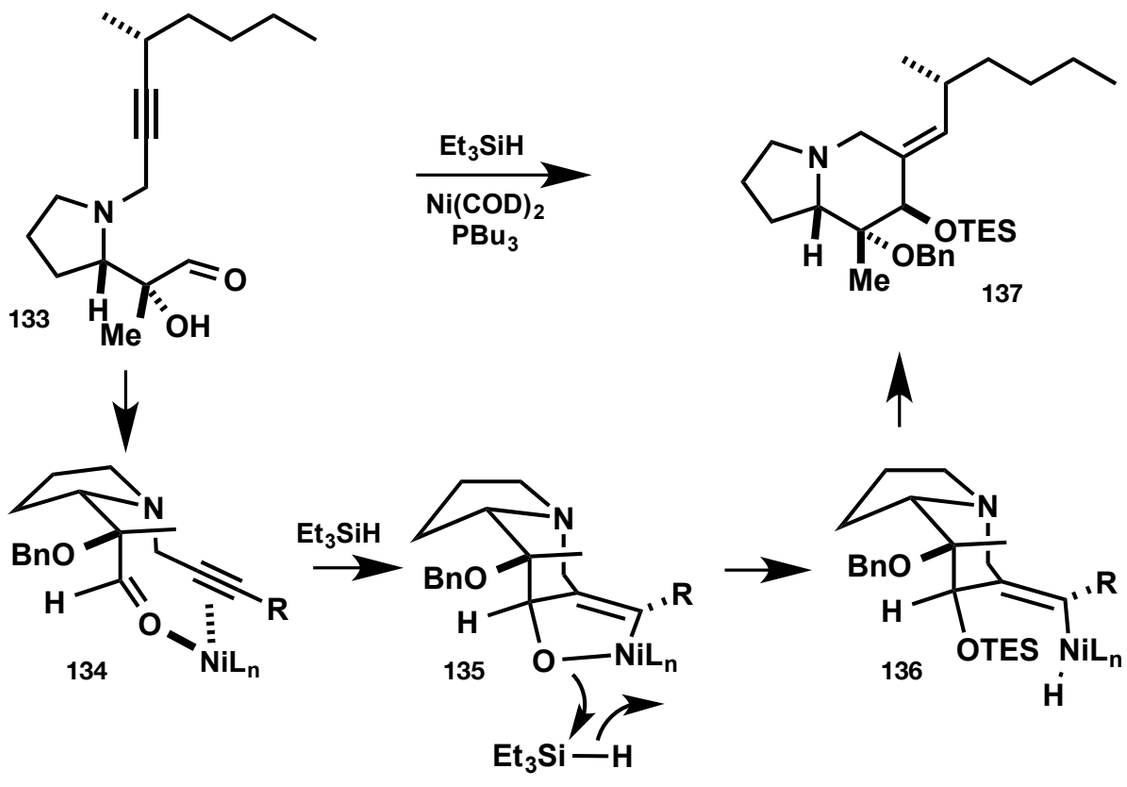
# Montgomery Group: (+)-Allopumiliotoxin



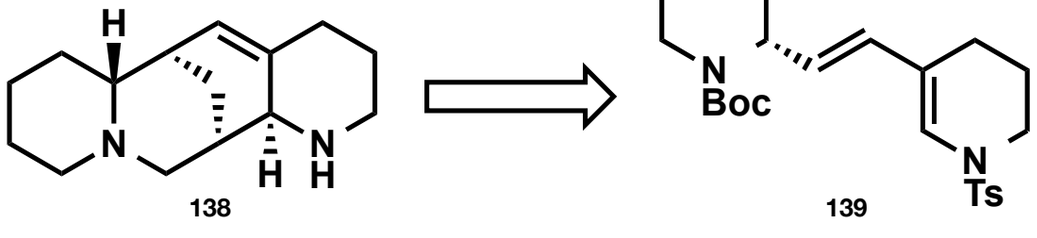

- Key step:

Nickel catalyzed reductive cyclization of ynals

*J. Am. Chem. Soc*. **1999**, *121, 6098-6099*.

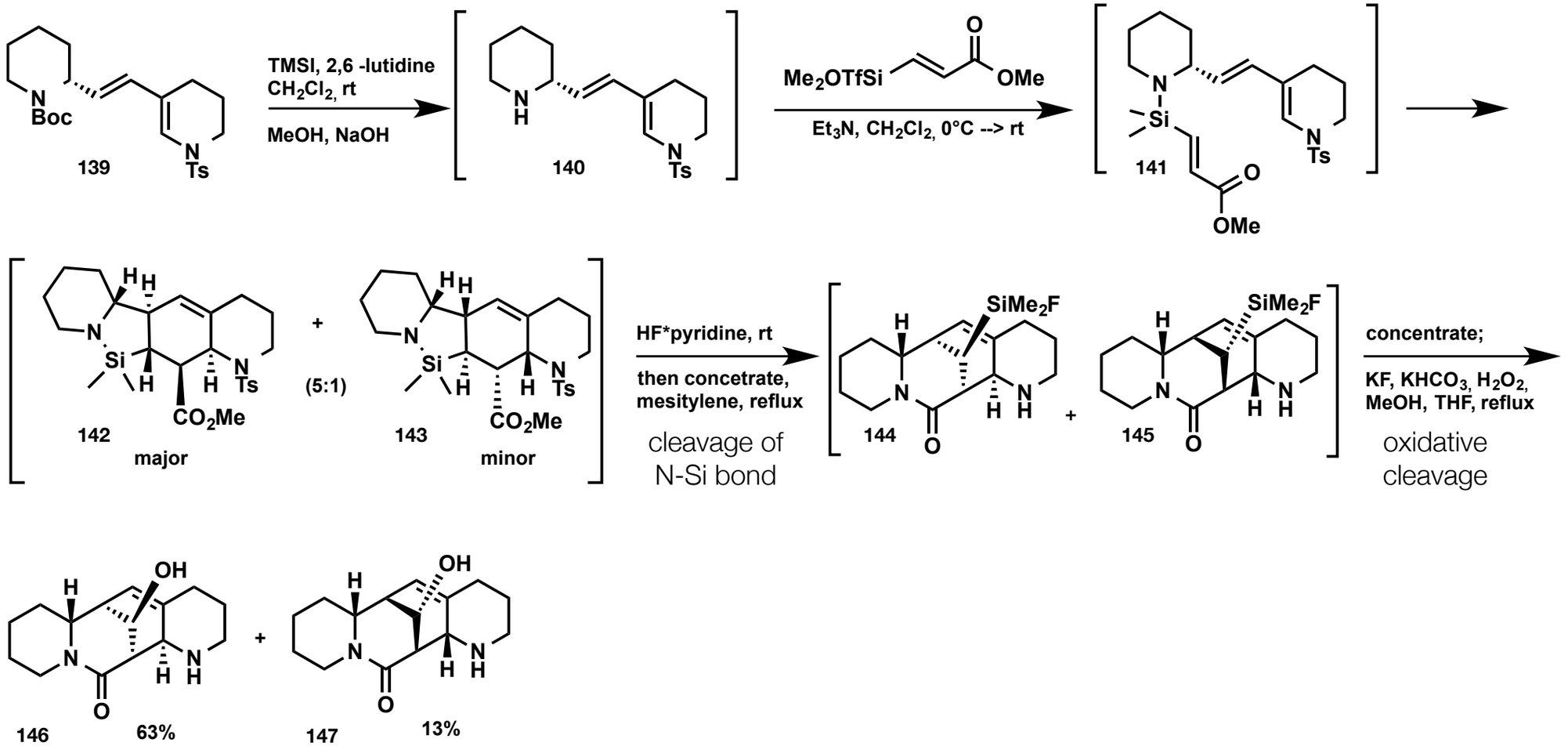


# Overman Group: (+)-Aloperine

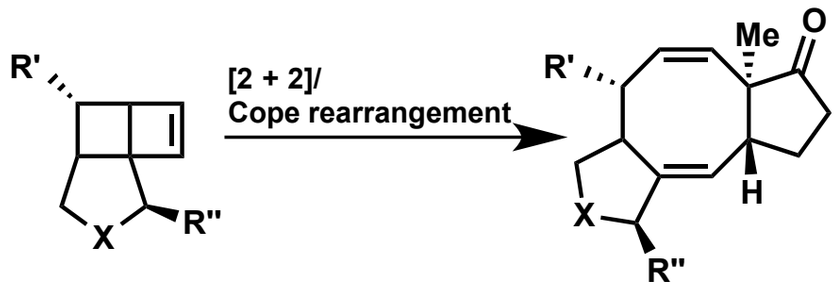



- Key step:
  Intramolecular Diels-Alder reaction with a nitrogen-bound silicon tether

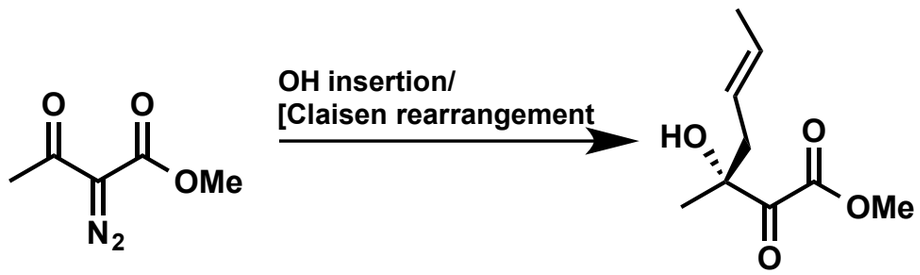
*J. Am. Chem. Soc.* **1999**, *121, 700-709*.



# Methodologies



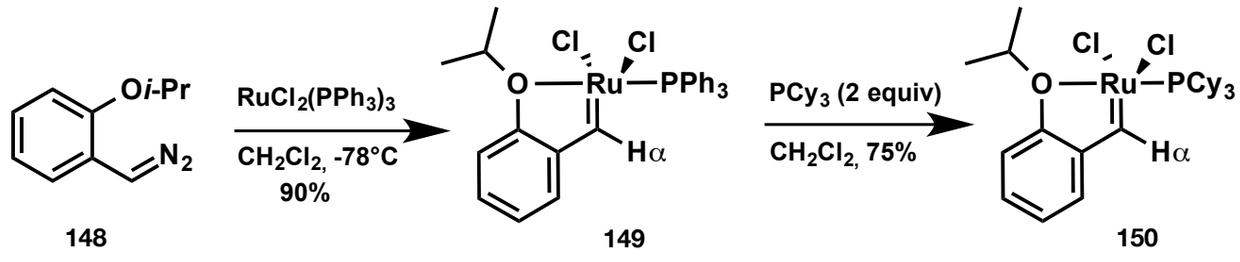

JACS 1999



# JACS 1999: Methodologies

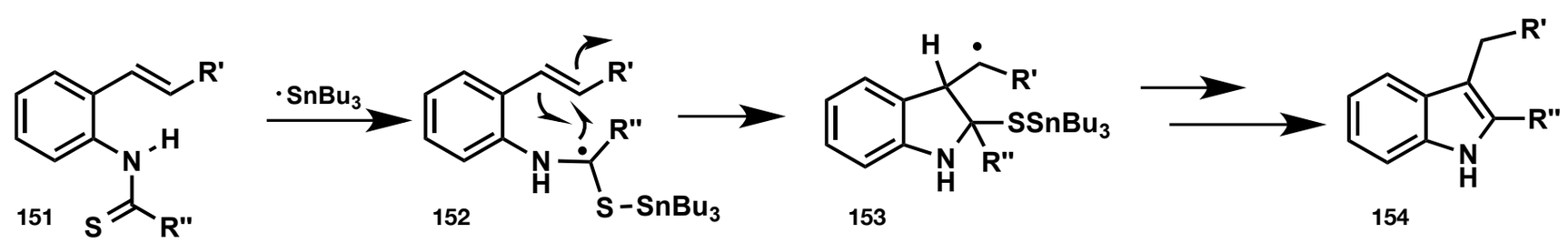
## 1) Hoveyda-Grubbs Catalyst (1999):

- exceptionally robust
- can be purified by simple silica gel column
- but also very expensive



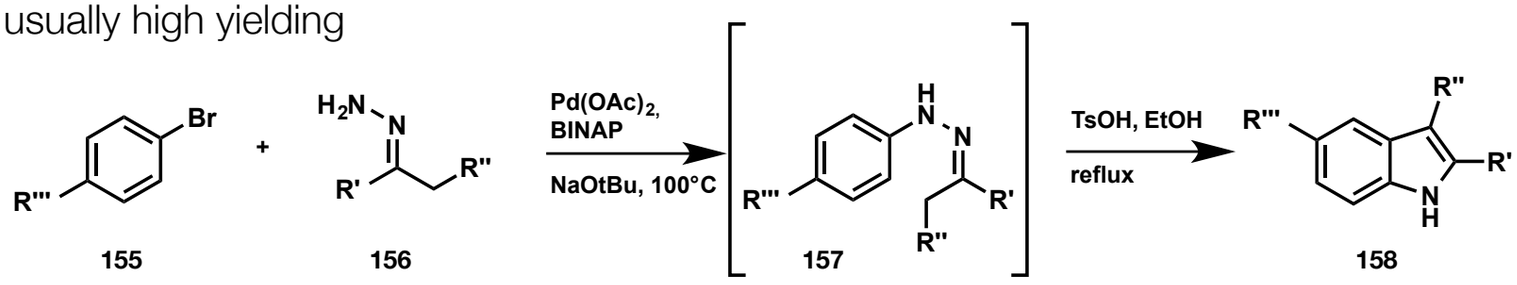

## 2) Fukuyama Indole synthesis: Radical Cyclization of 2-Alkenylthioanilides to 2,3-disubstituted Indoles

- under very mild radical conditions
- has been applied to the total synthesis of aspidophytine, vinblastine and strychnine




## 3) Buchwald Indole synthesis: Palladium-catalyzed Preparation via Fischer Indole Synthesis

- extends the Fischer-Indole Synthesis to broad variation of ketones
- usually high yielding



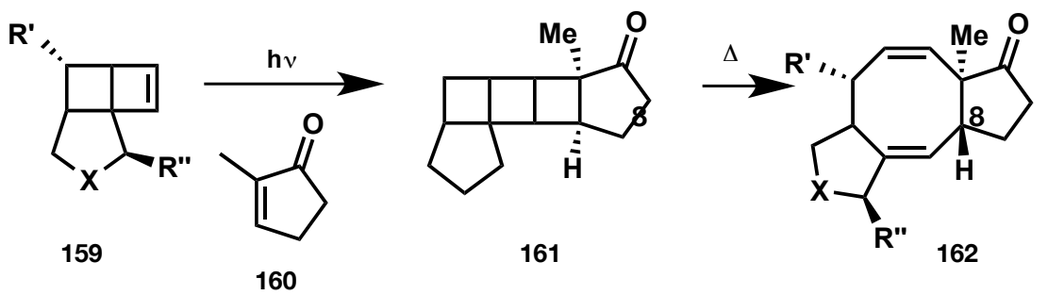


(1) Hoveyda, A. H. J. *Am. Chem. Soc.,* 1999, 121, 791–799.
(2) Fukuyama, T. *J. Am. Chem. Soc*., 1999, 121, 3791-3792.
(3) Buchwald, S. L. *J. Am. Chem. Soc*., 1999, 121, 10252-10263.

# [2+2] Photocycloaddition/Thermal Retrocylcoaddition

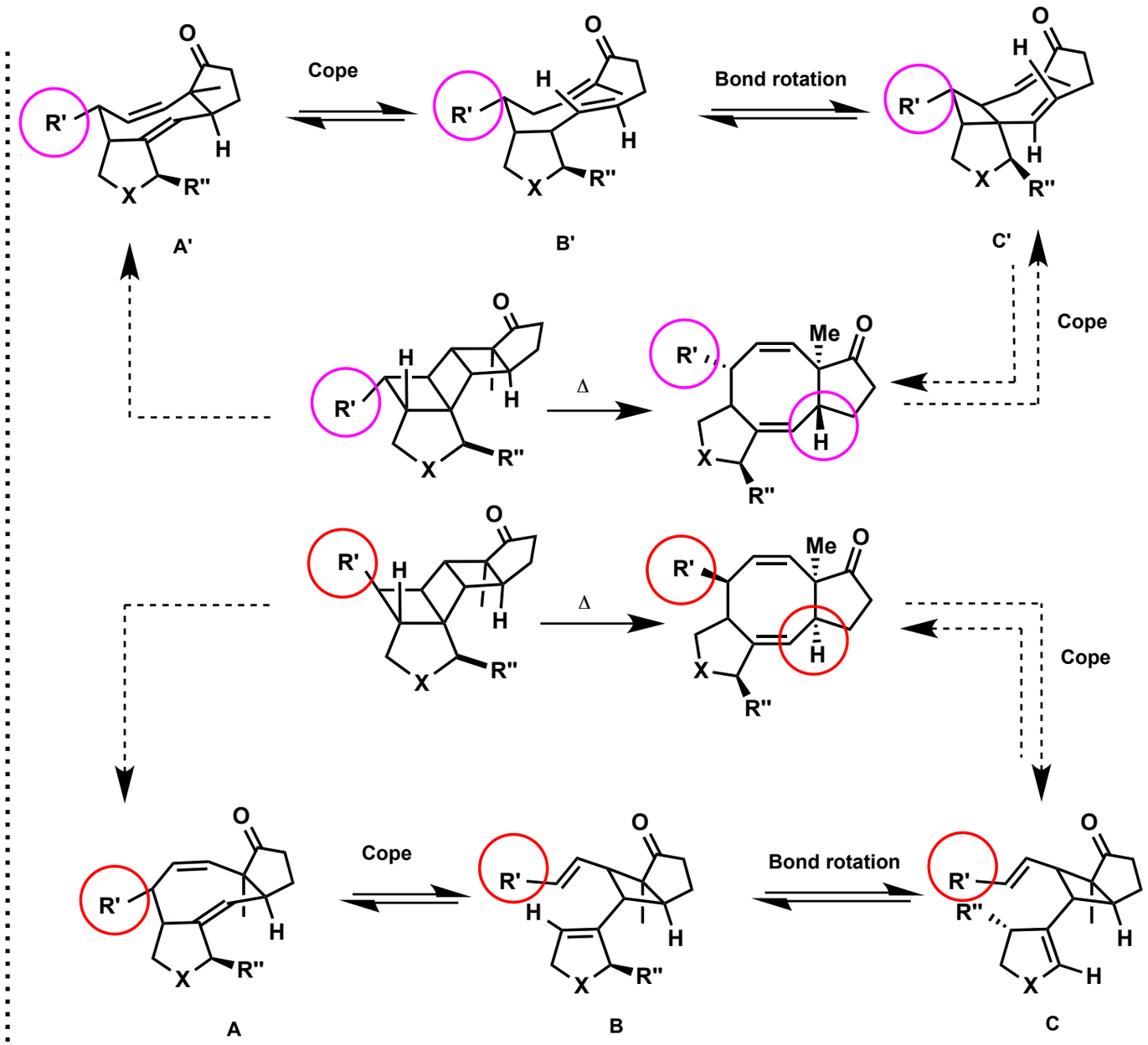
## A new entry into functionalized 5-8-5 Ring systems

- Cyclopentenones as versatile substrates
- R’ = Me : only one regioisomer for the [2+2]
- Inversion of stereochemistry at C-8




X = C, O
R' = Pr, $CO_2Me$
R'' = Me, OH

## Proposed Mechanism:

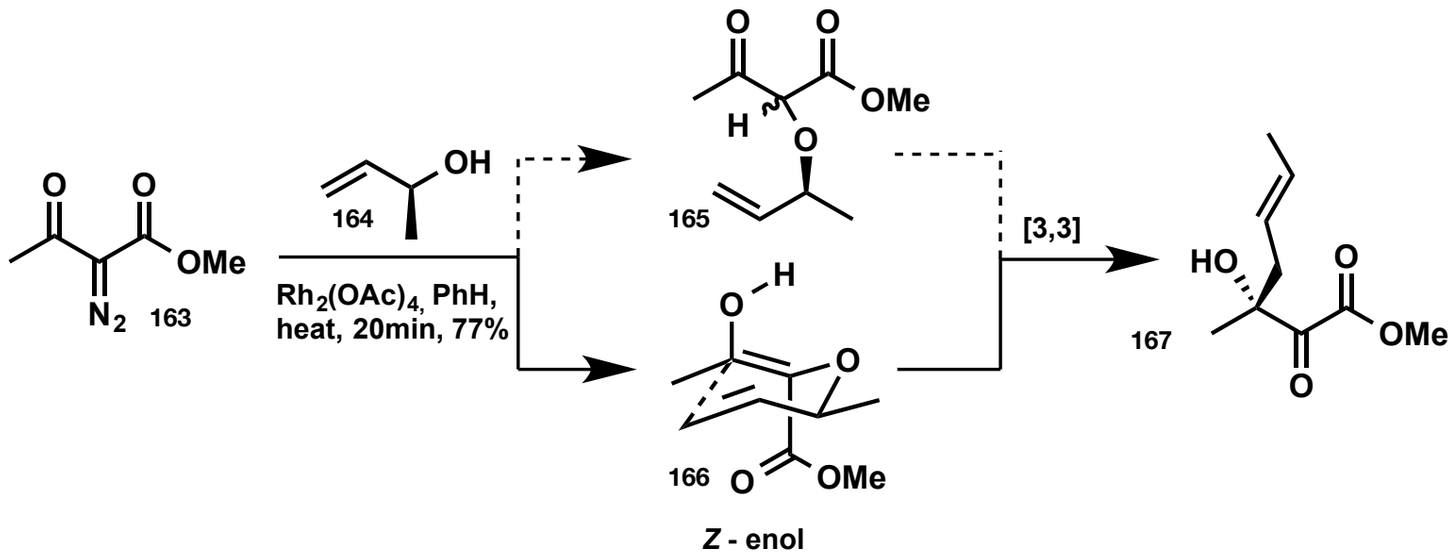



(1) M. L. Snapper *J. Am. Chem. Soc.* **1999**, *121*, 4534-4535.

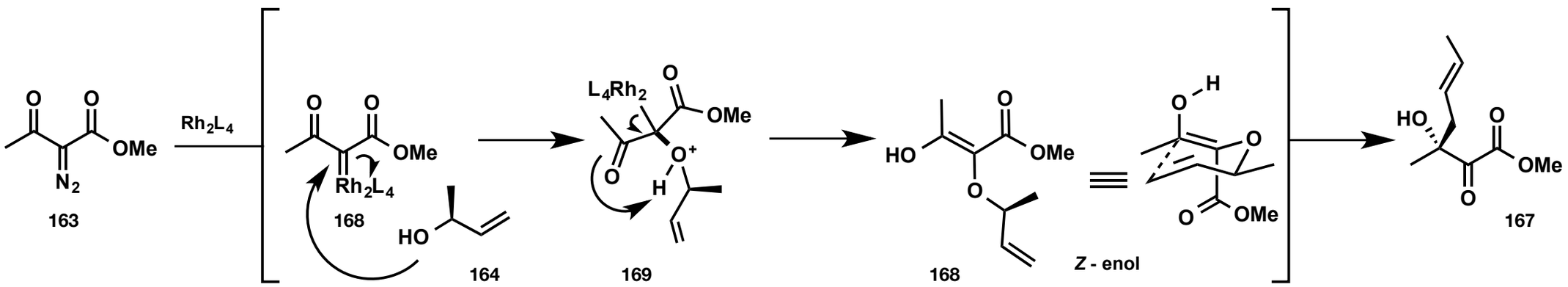
# Rhodium Carbenoid-initiated Claisen Rearrangement

## Synthesis of alpha-Hydroxy Carbonyl Compounds

- stereoselective formation of tertiary alcohols through a tandem O-H insertion/[3,3] rearrangement process
- the observed intermediate is not the ketone whereas the (*Z*) enol ether is formed




Revealed mechanism:




(1) J. L. Wood *J. Am. Chem. Soc.* **1999**, *121*, 1748-1749.

Thank you for your kind attention!