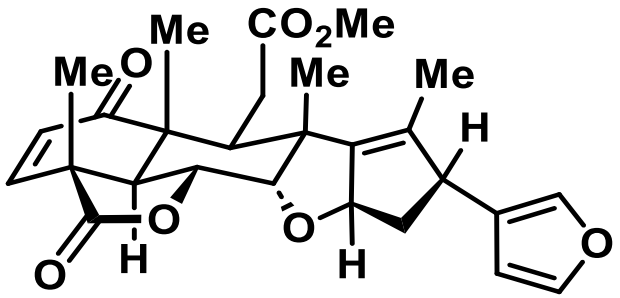
Stereoselective Total Synthesis of Nimbolide

2025. 09.11

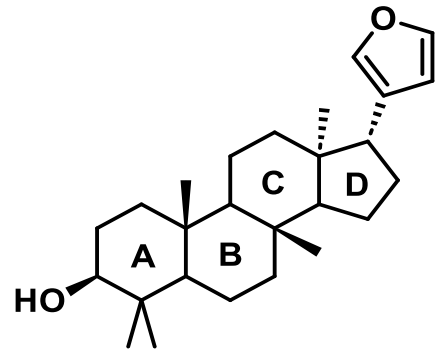
张丰博



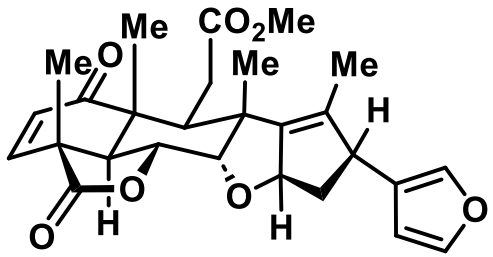
nimbolide

Introduction of C-seco limonoids

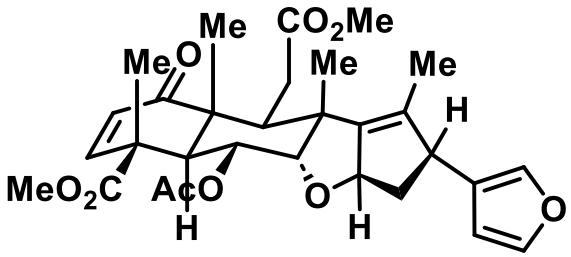
- **C-seco limonoids**
- Many C-seco limonoids have been found to possess potent antifeedant, anticancer, and antimetastatic activity.



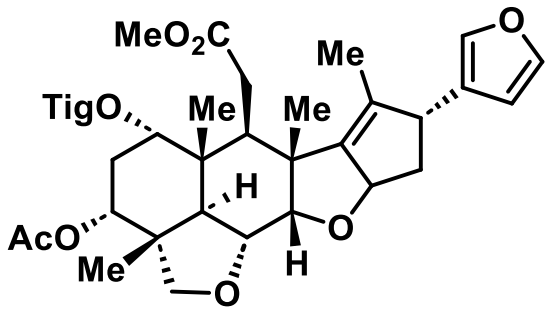
limonoids



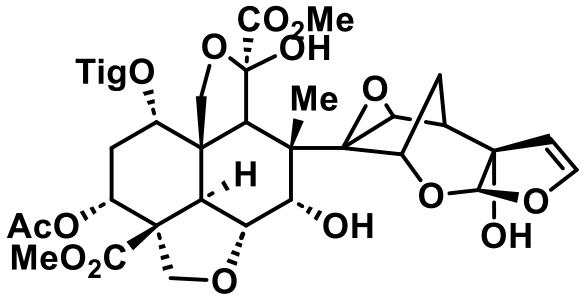
nimbolide



nimbin



salannin



azadirachtin

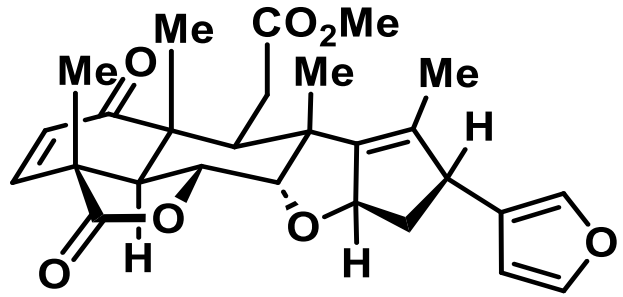
Introduction of Author

- **David Sarlah**
- David Sarlah was born and raised in Slovenia, where he obtained his Bachelor's Degree in Chemistry at the University of Ljubljana.
- carried out his undergraduate research with Prof. K. C. Nicolaou at Scripps and Prof. Samuel J. Danishefsky at Columbia.
- obtained his Ph.D. in chemistry with Prof. K. C. Nicolaou involving the total synthesis of complex natural products.
- joined Prof. Erick M. Carreira's group at ETH as a postdoctoral fellow and explored the field of asymmetric catalysis.
- In 2014, David joined the faculty at the University of Illinois, Urbana-Champaign, and moved to Rice University in 2024.

https://cn.chem-station.com/chemists/2018/12/david-sarlah.html
https://orcid.org/0000-0002-8736-8953
https://chem.whu.edu.cn/info/1277/58741.htm

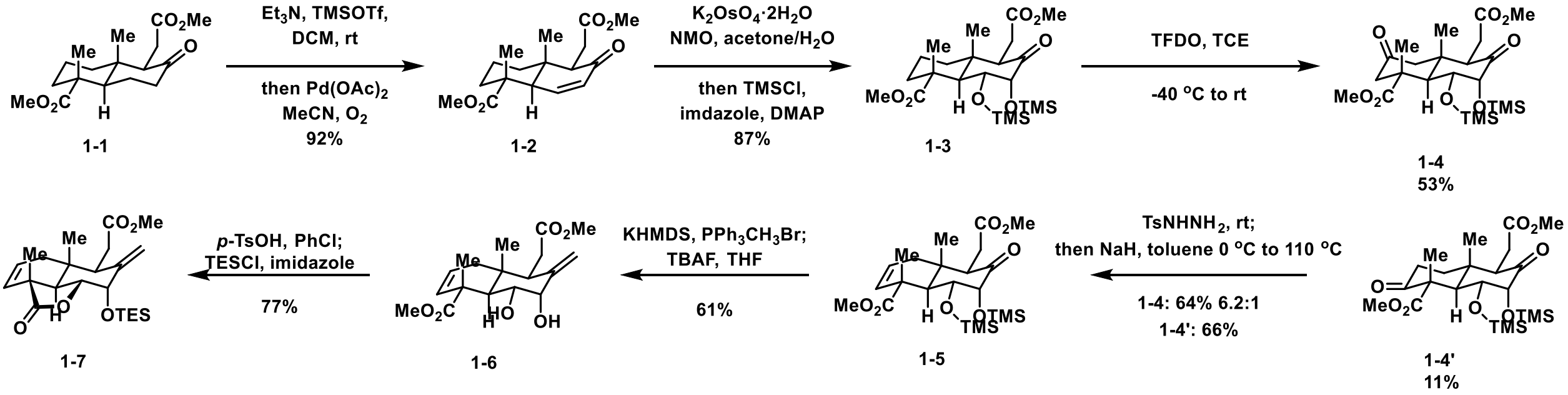
Features of Nimbolide

- a highly oxidized trans-decalin core
- an equatorially disposed carboxylic ester derivative at C(4),
- a fused tetrahydrofuran (THF) ring
- an oxidatively sensitive furan motif



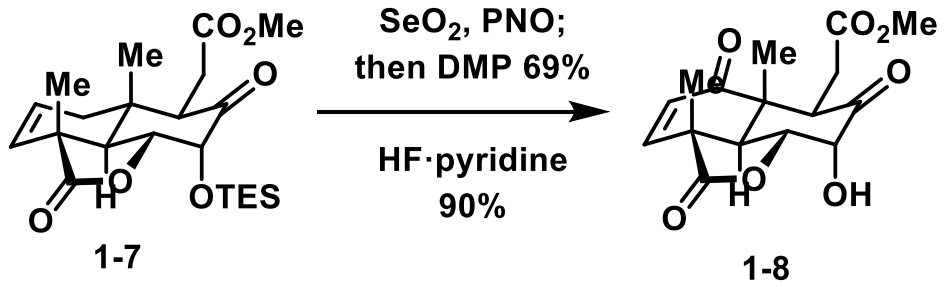
nimbolide

Previous Synthesis of Nimbolide

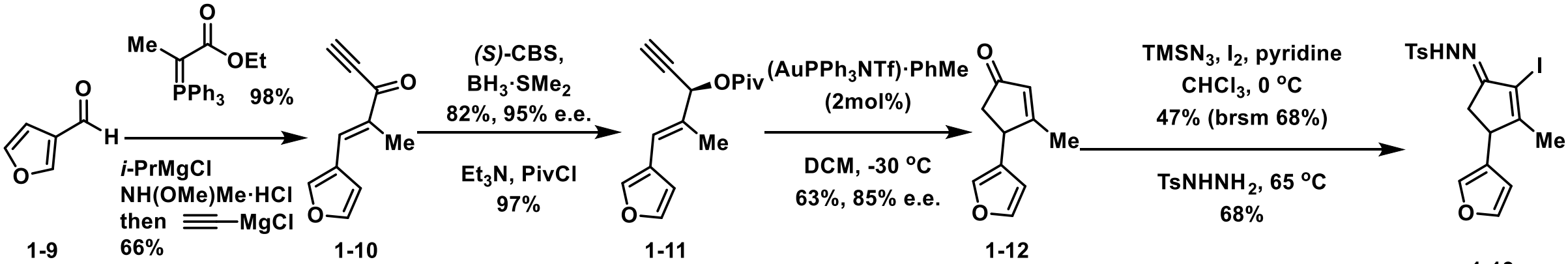


https://doi.org/10.1038/s44160-023-00437-w

Previous Synthesis of Nimbolide



1-7 1-8



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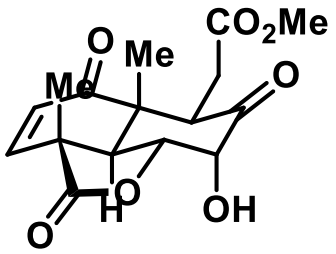
Previous Synthesis of Nimbolide



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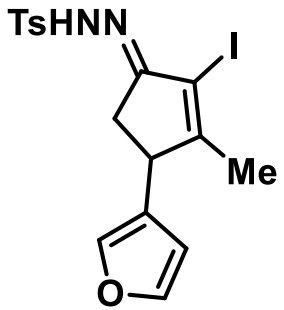
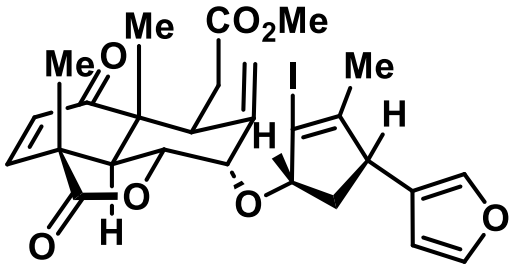


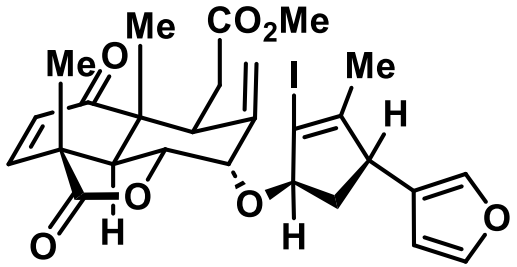
1-13

K_2CO_3, PhF

140 °C



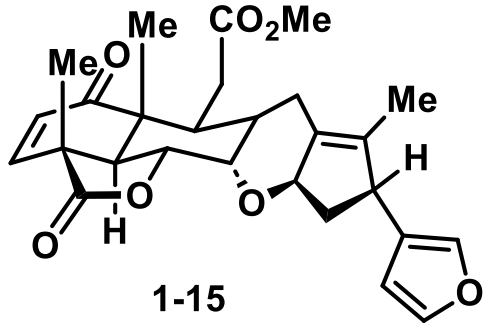
1-14'
31%



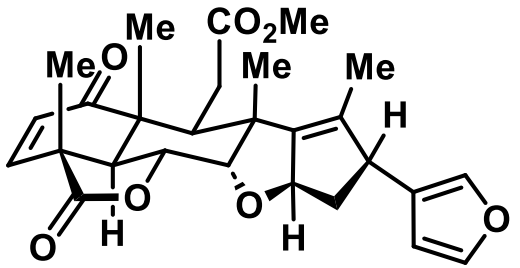
1-14
43%

AIBN, *n*-Bu_3SnH

C_6F_6, 80 °C

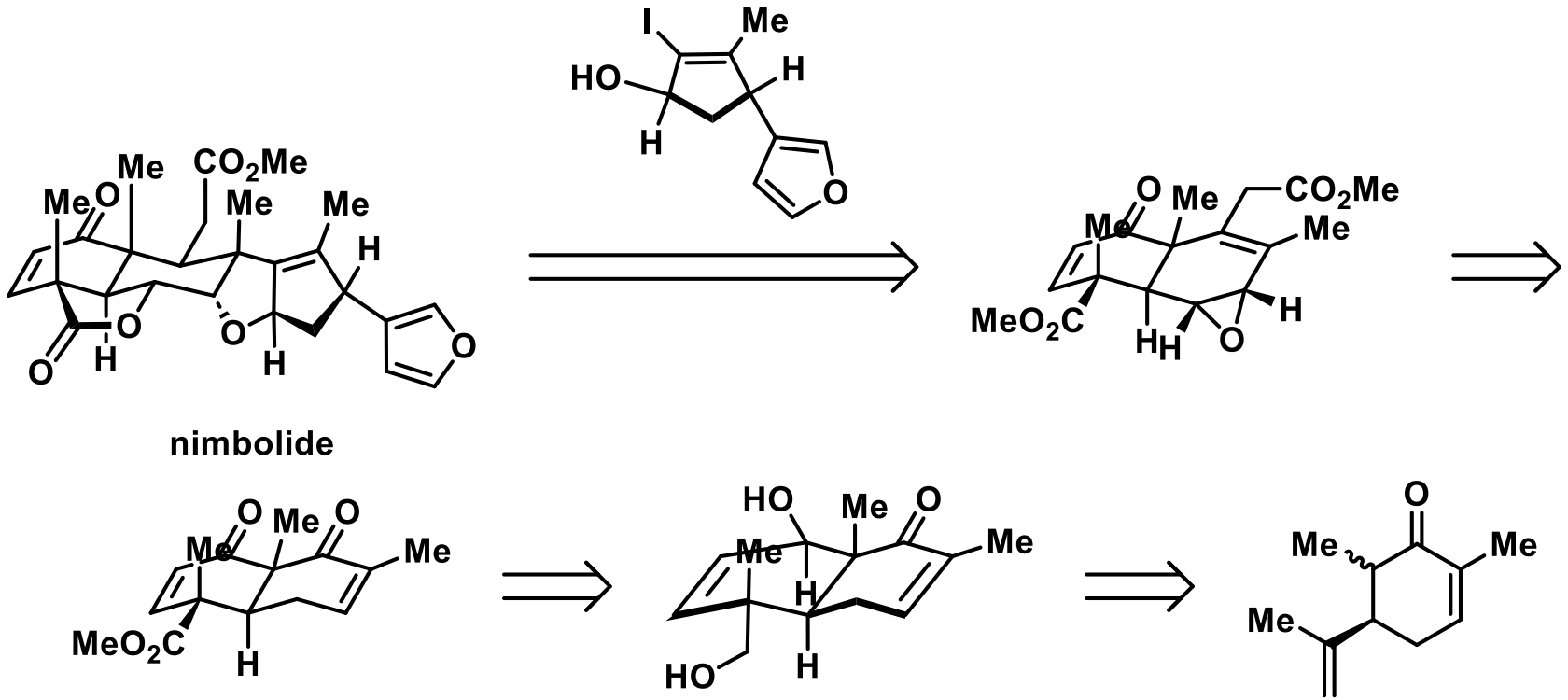


1-15
23%



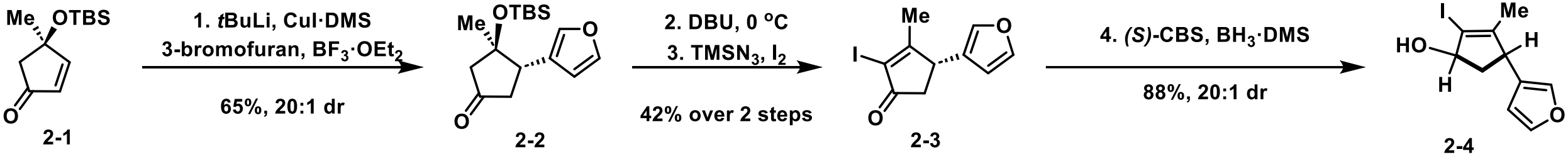
nimbolide
45%

Retrosynthetic Disconnections

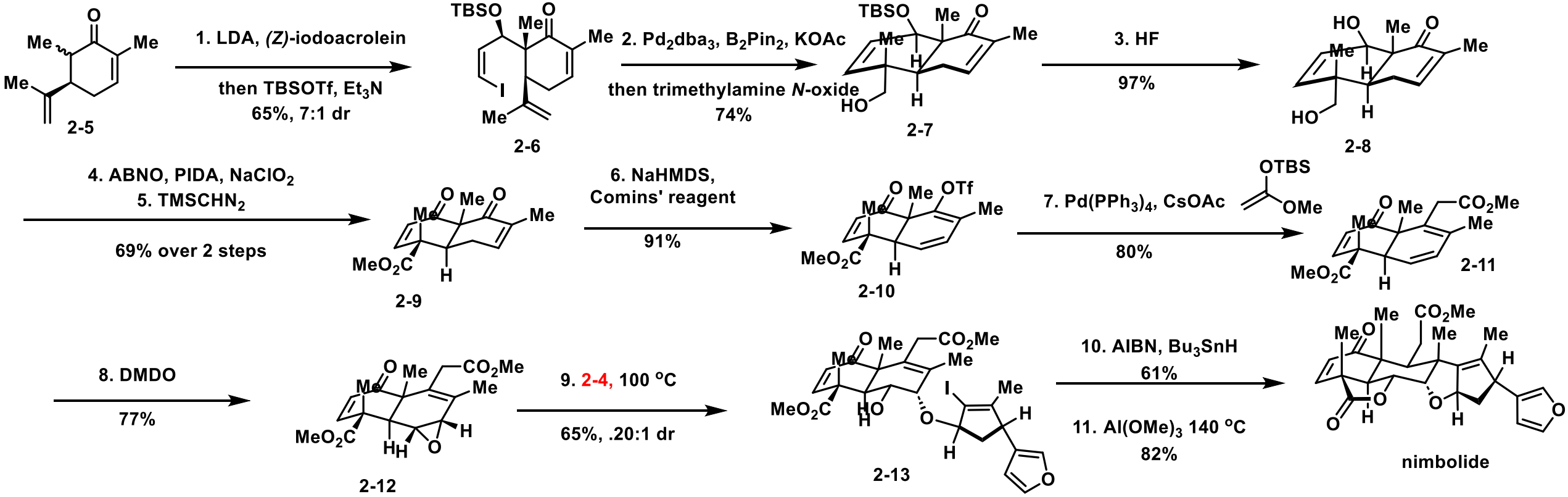


nimbolide

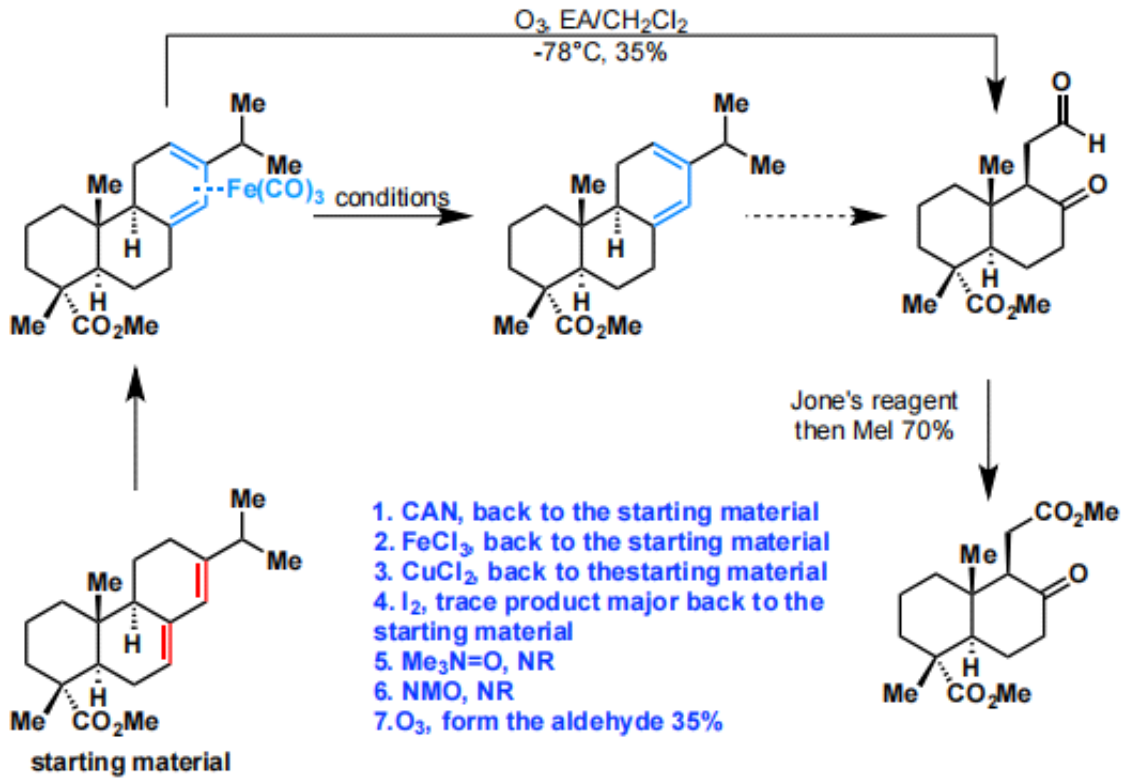
Synthesis of Nimbolide



Synthesis of Nimbolide



补充



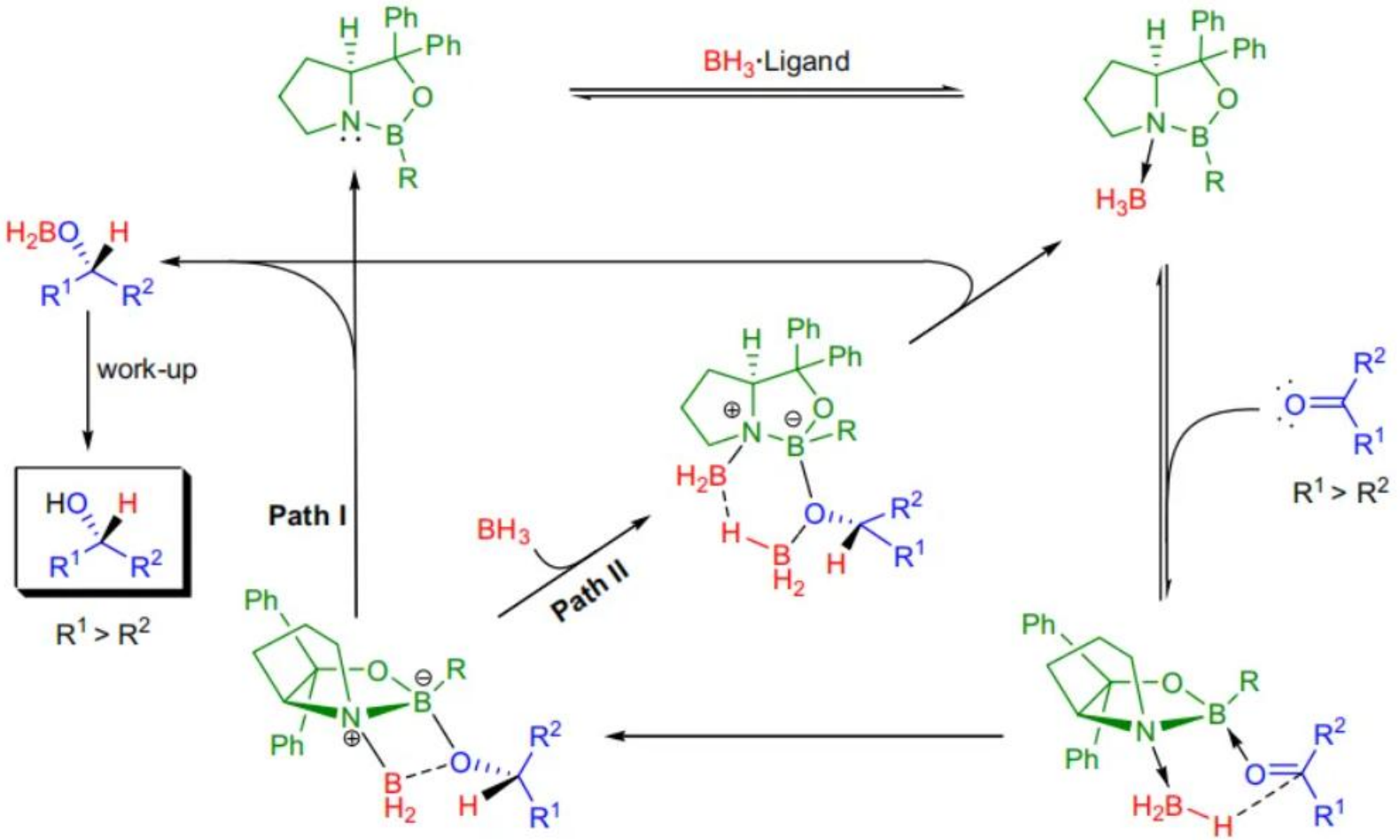
Scheme S2. Oxidative cleavage of the iron complex[1]

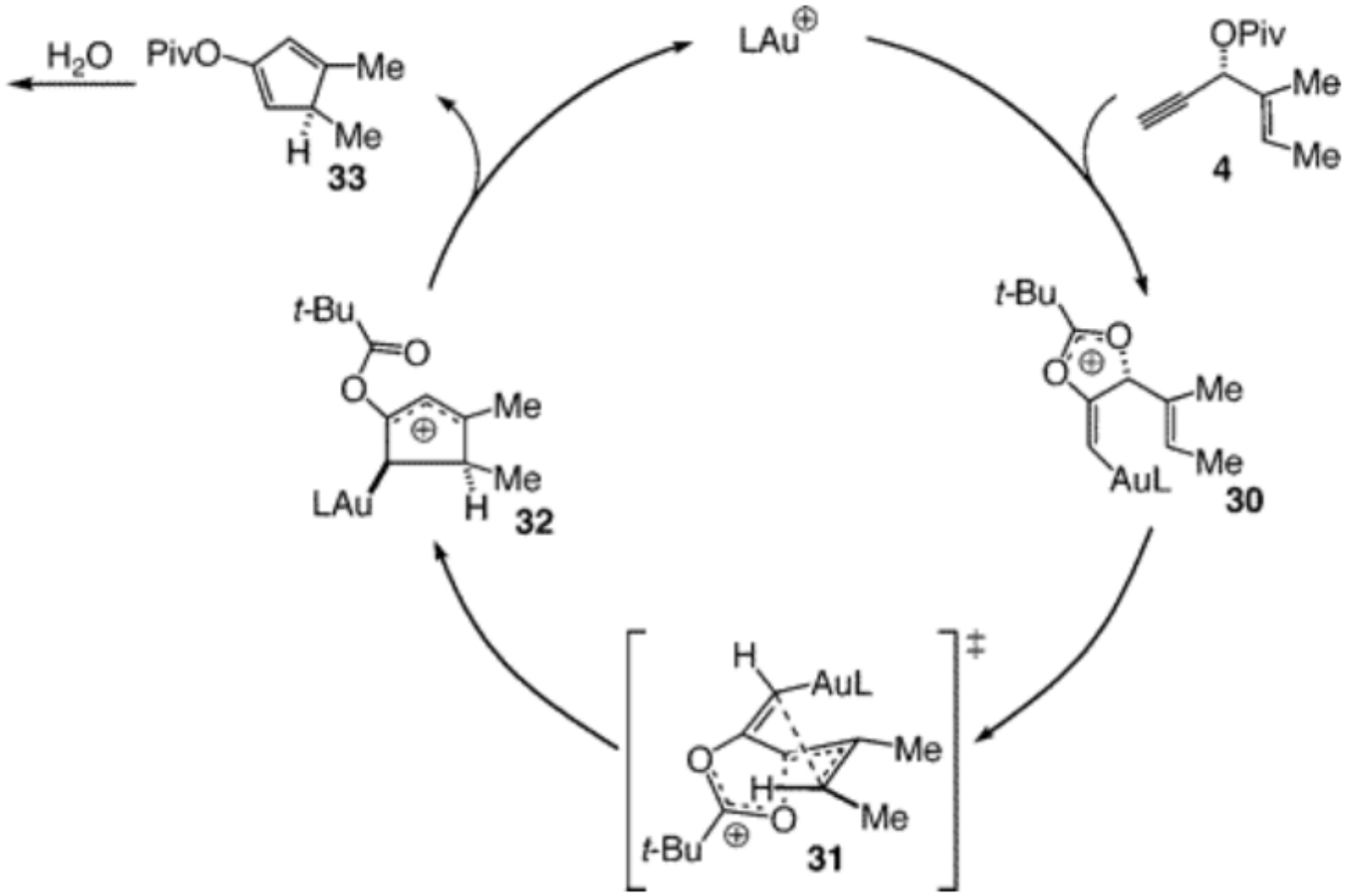
补充


Me3Si–OOH
Me3Si–OAc
AcO Pd0 –H
AcO–PdII-OAc
TMSO
1
Coordination
AcO–Pd–OAc
TMSO
2
Me3Si–OAc
AcO–Pd
O
3
Oxoallyl-Palladium Complex.
β-hydride elimination
AcO–Pd–H
O
4
O
5
Palladium hydride enone complex
Saegusa-Ito Oxidation

补充

Corey-Bakshi-Shibata还原反应




LAu⊕
OPiv
Me
Me
4
t-Bu
O
O
Me
AuL
Me
30
H
AuL
Me
O
H
O
Me
t-Bu⊕
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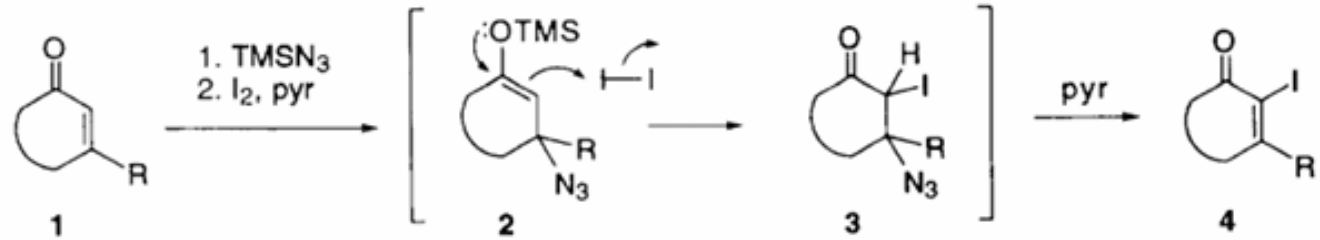
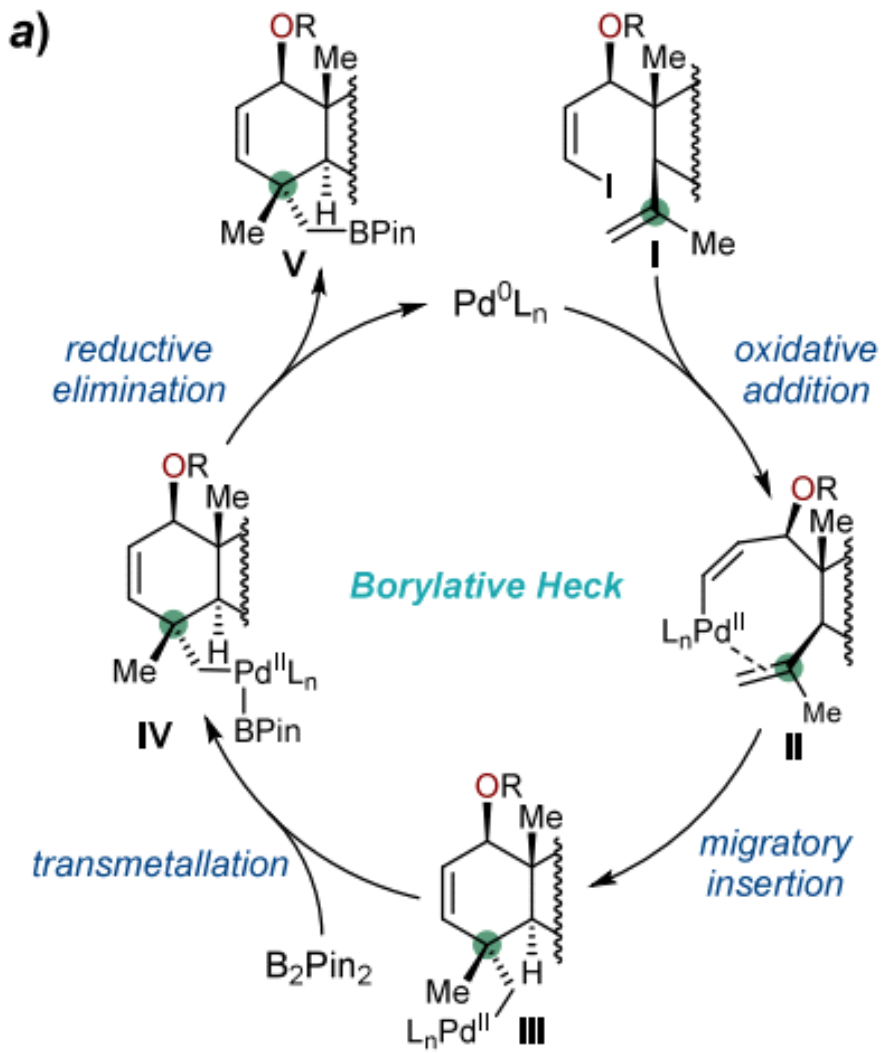
H2O
PivO
Me
H
Me
33


O
R
1
1. TMSN3
2. I2, pyr
:OTMS
I
R
N3
2
O
H
I
R
N3
3
pyr
O
I
R
4

补充


a)
OR
Me
Me
H
BPin
V
OR
Me
I
Me
I
Pd0Ln
reductive elimination
oxidative addition
OR
Me
Borylative Heck
LnPdII
Me
II
OR
Me
Me
H
PdIILn
BPin
IV
transmetallation
migratory insertion
OR
Me
B2Pin2
Me
H
LnPdII
III

补充内容

- 1、六元环的绘制考虑直立键与平伏键的交错问题，相邻不会全是向里/外，存在不饱和键时结构需要保持合理，不均为椅式构象。
- 2、化学/区域/立体选择性，也许需要从基础再了解有机化学一遍
- 3、分子内反应要快于分子间反应，分子内结构相对单一，克服的分子间作用力较小，在空间上反应的位点更近，使得钯催化先发生迁移插入再与硼进行转金属化
- 4、二甲基二氧代环丙烷通过均裂形成自由基氧化碳氢键
- 5、在非质子溶剂中，重氮化合物释放氮气生成卡宾，卡宾插入到氧氢键之间生成碳氧键
- 6、格氏试剂与酰胺反应相比酯更困难，格氏试剂与酯反应会快速生成三级醇，而与酰胺反应可以终止在羰基酮。氧比氮更易离去。