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Communication

Asymmetric Total Synthesis of Bufospirostenin A

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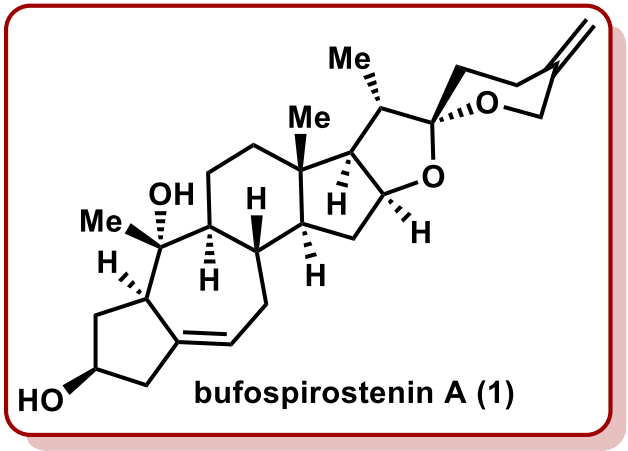


bufospirostenin A (1)

This Work:

First total synthesis via Pauson-Khand reaction

Reporter: Fusong Wu

Supervisors: *Prof.* Tao Ye, *Dr.* Yian Guo

2020.7.20

学习经历：

♦2006.08-2008-05

Scripps研究所，博士后 导师：P.Baran

♦2001.09-2006.07

北京大学，博士 导师：杨震

♦1997.09-2001.07

中国农业大学，学士

工作经历：

- ♦ 2013--现在 南方科技大学，化学系，教学副系主任，副教授、教授
- ♦ 2008 -2013 北京大学，深圳研究生院，副教授，博士生导师

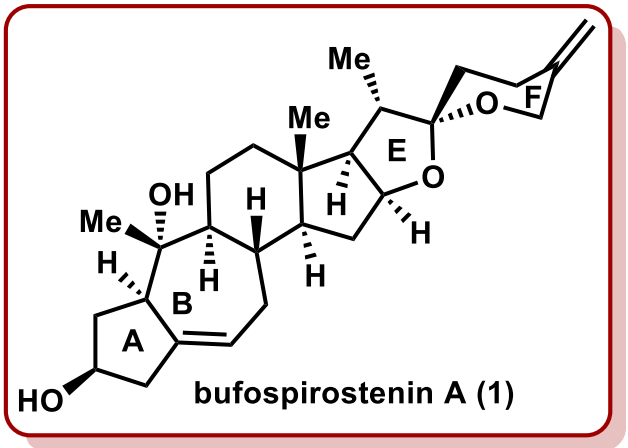
研究方向：

♦复杂活性天然产物全合成研究；

♦导向天然产物的新颖合成方法学研究；

♦天然产物的化学生物学及药物化学研究。

Background



bufospirostenin A (1)

Isolation:

♦Isolated by Ye and co-workers in 2017 and obtained only 1.9 mg from the toad Bufo bufo gargarizans;

Biological activities：

♦possess a cardioactive effect and promote blood circulation through causing a 43% inhibition of Na/K ATPase (NKA) at 25 μM

Structural features：

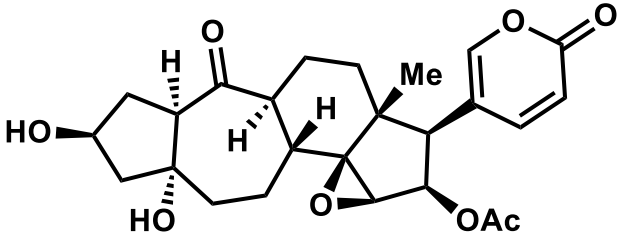
♦Unusual [5-7-6-5-5-6] ring system

♦ rearranged A/B ring system rather than the usual decalin system

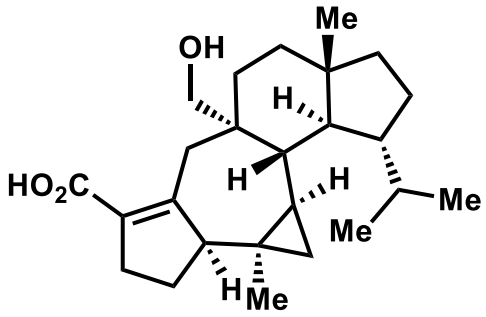
♦11 Stereocenters: 10 contiguous, two quaternary, one spiroketal

Tian, H. Y., Ye, W. C. et. al. *J. Nat. Prod.* **2017**, *80*, 1182–1186.

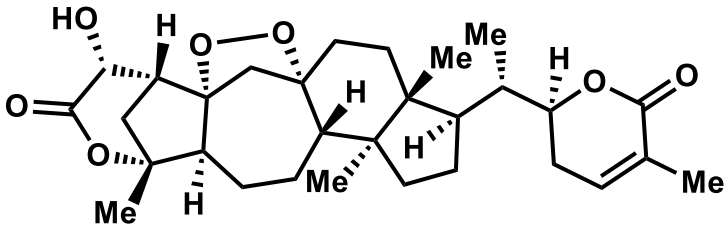
Background



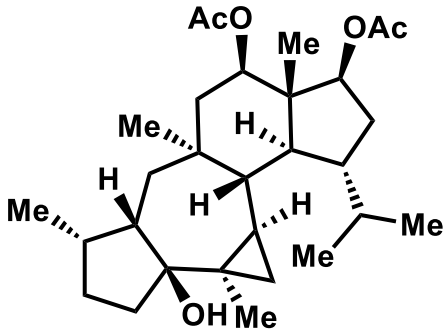
bufogargarizin B (2)



asperterpenoid A (3)

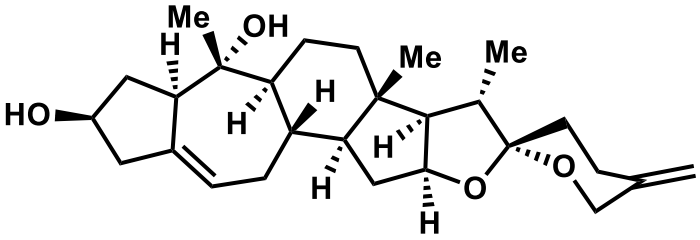


schinalactone A (4)

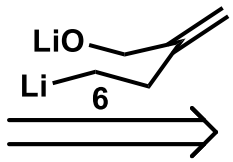


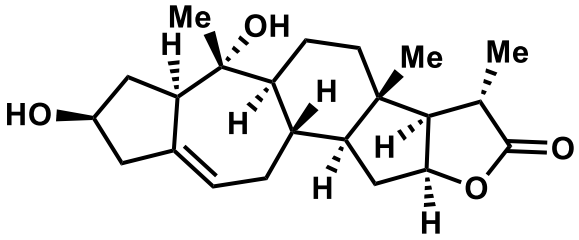
gypmacrophin A (5)

Retrosynthetic Analysis of Bufospirostenin A



bufospirostenin A (1)





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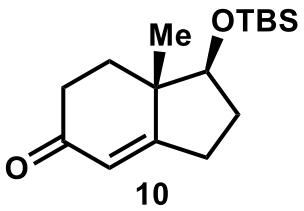
FGI



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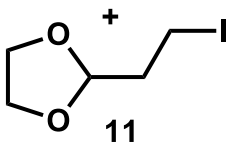

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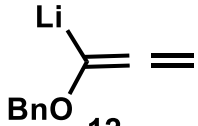

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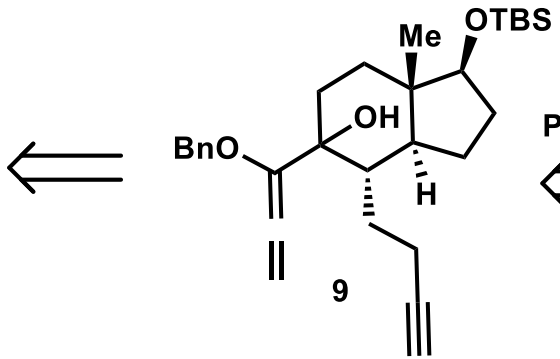

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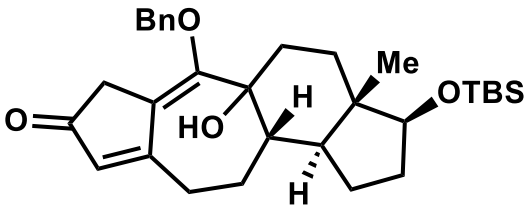
Pauson-Khand



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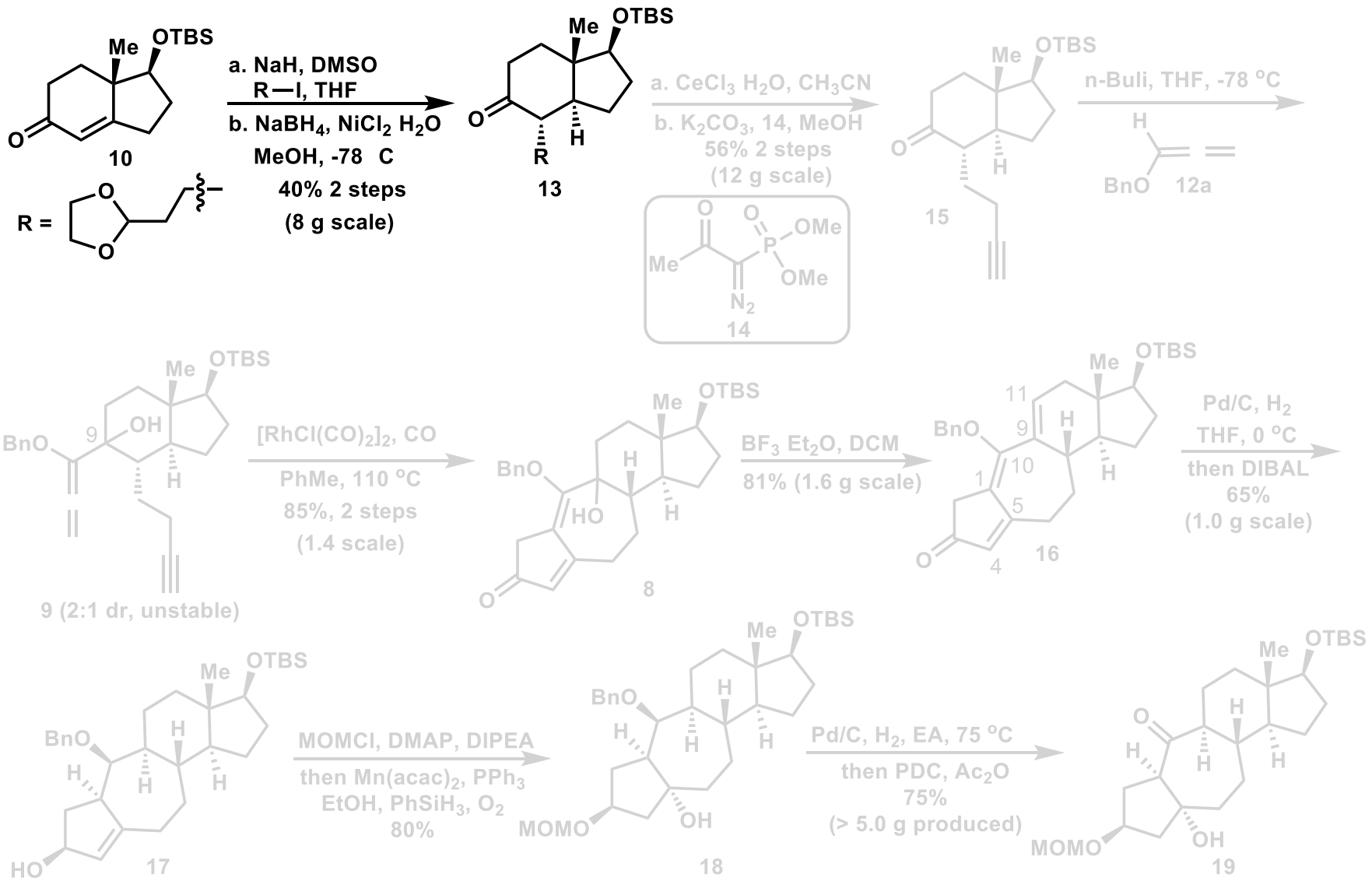
Asymmetric Synthesis of 19



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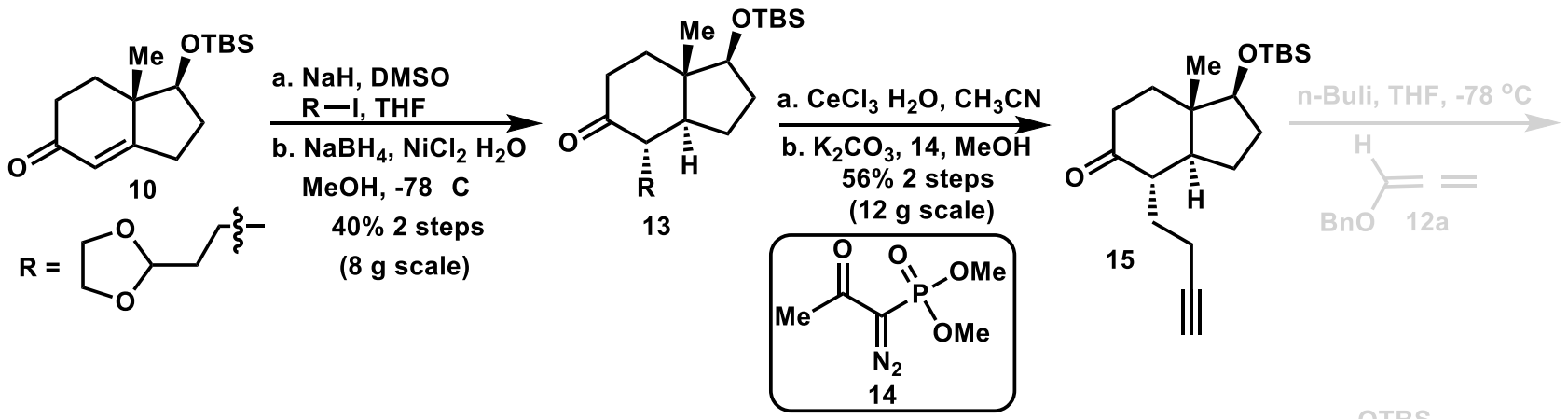

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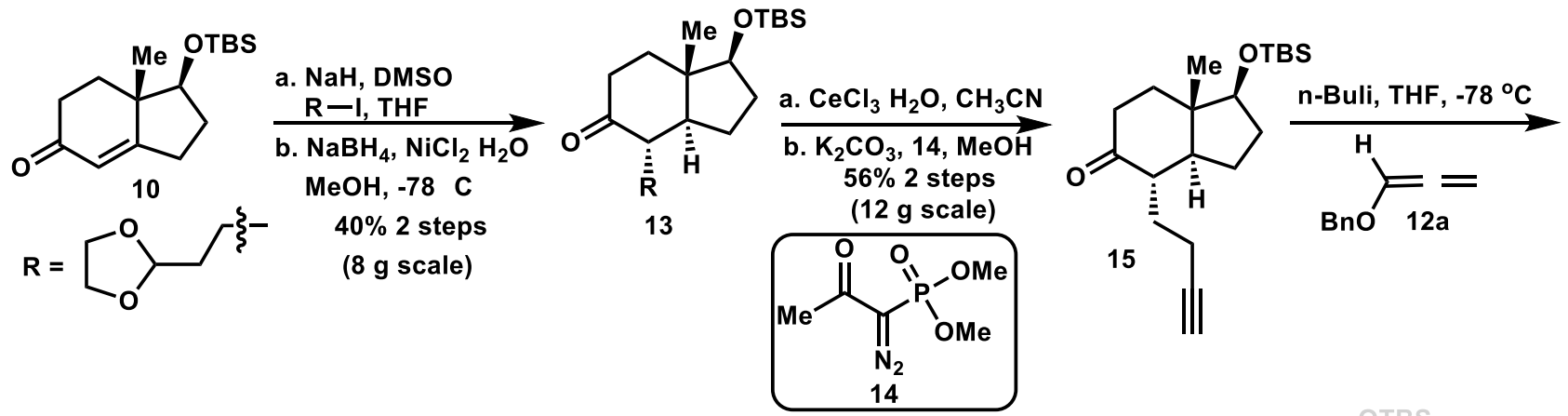

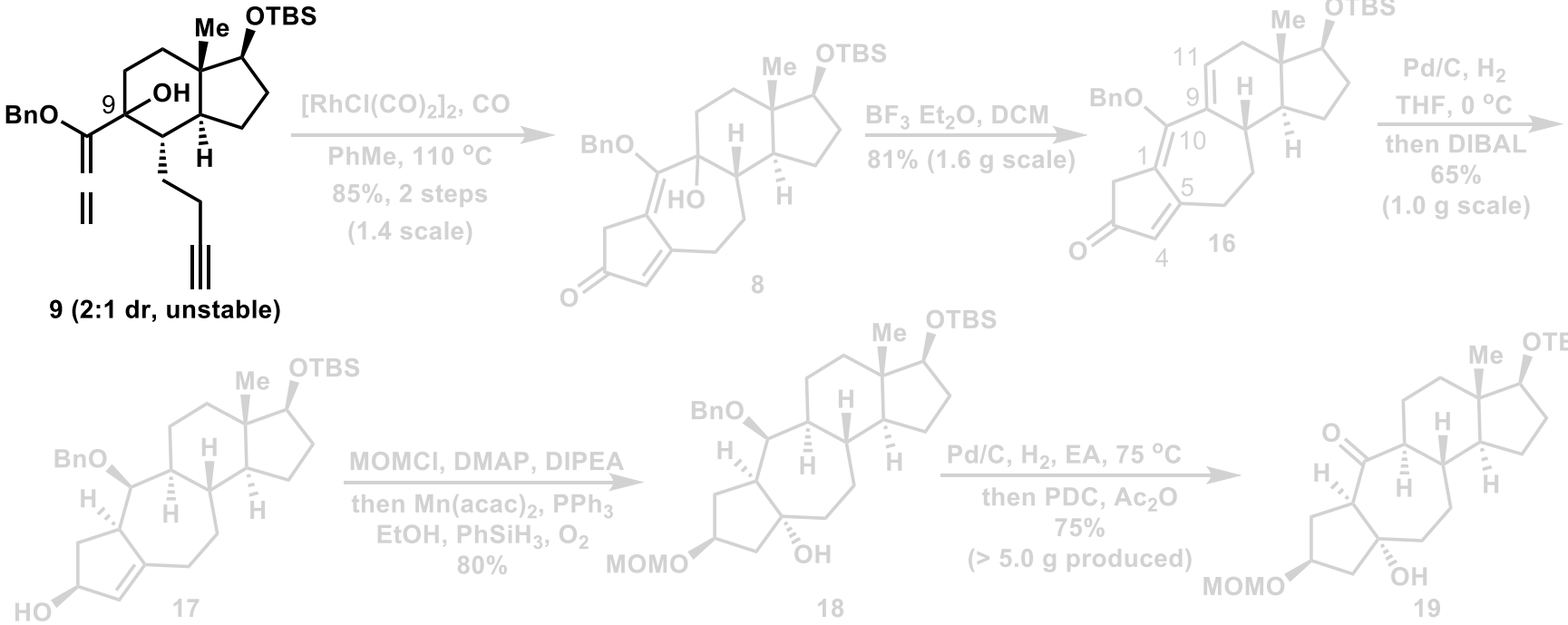

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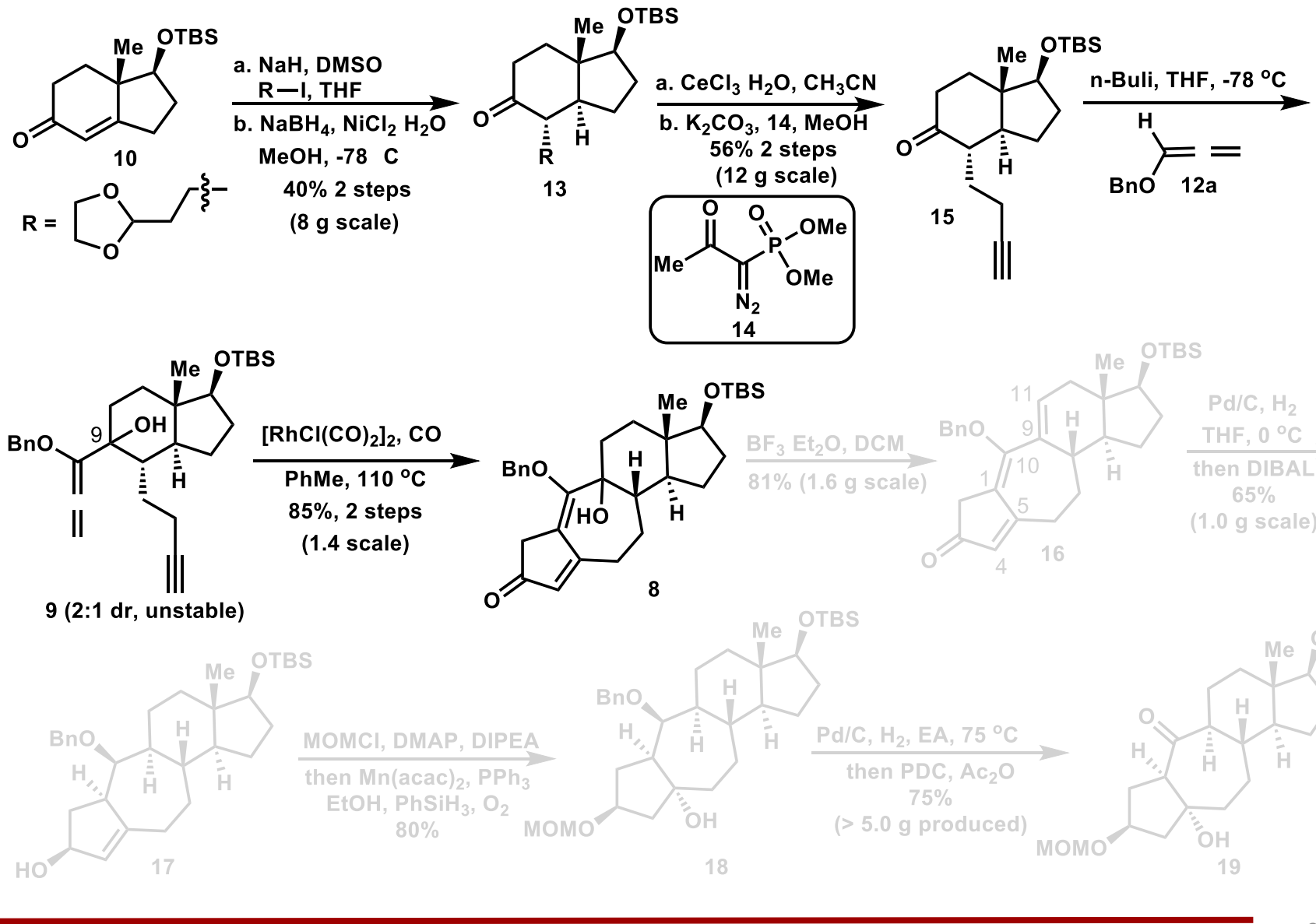

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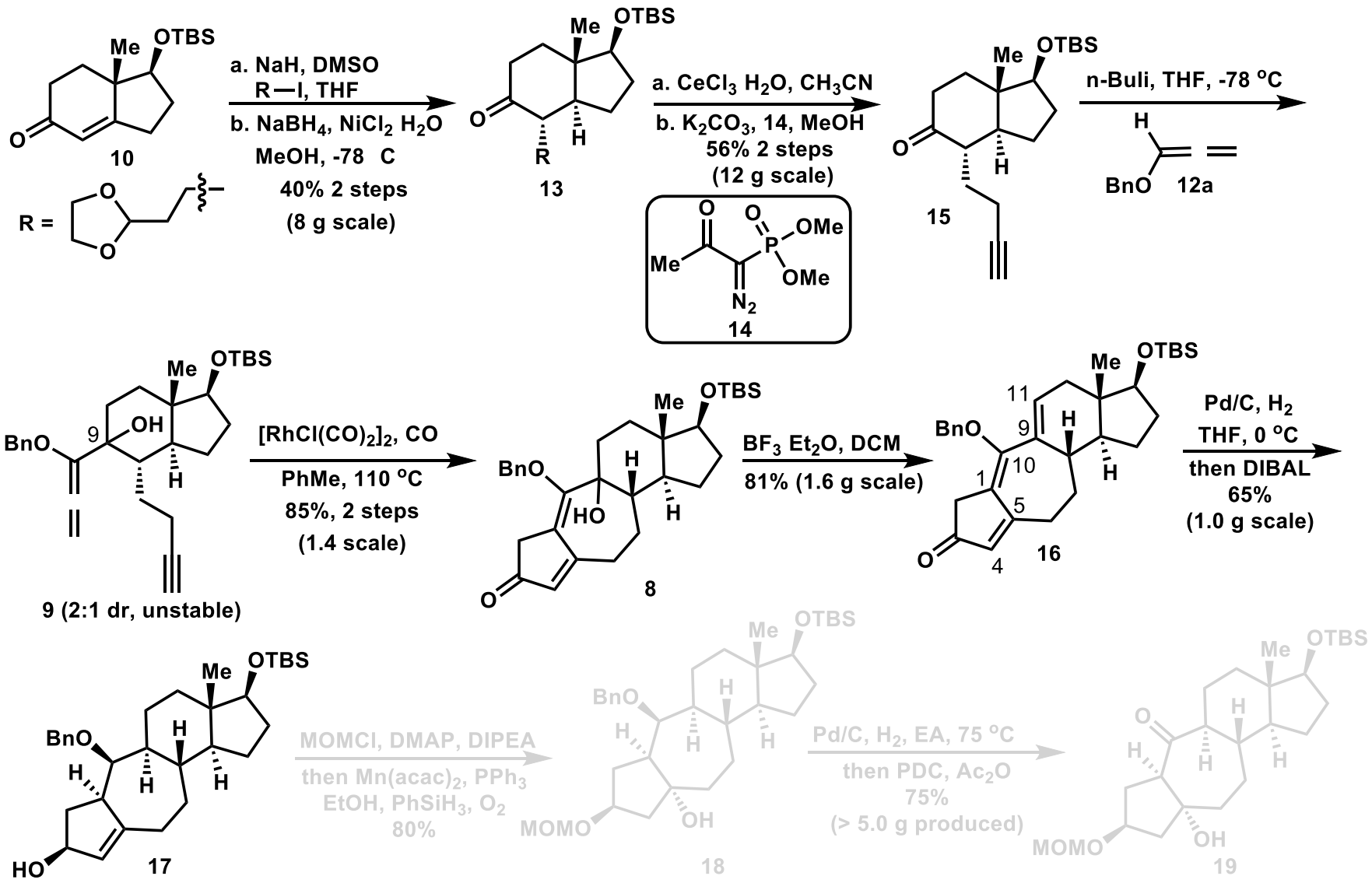

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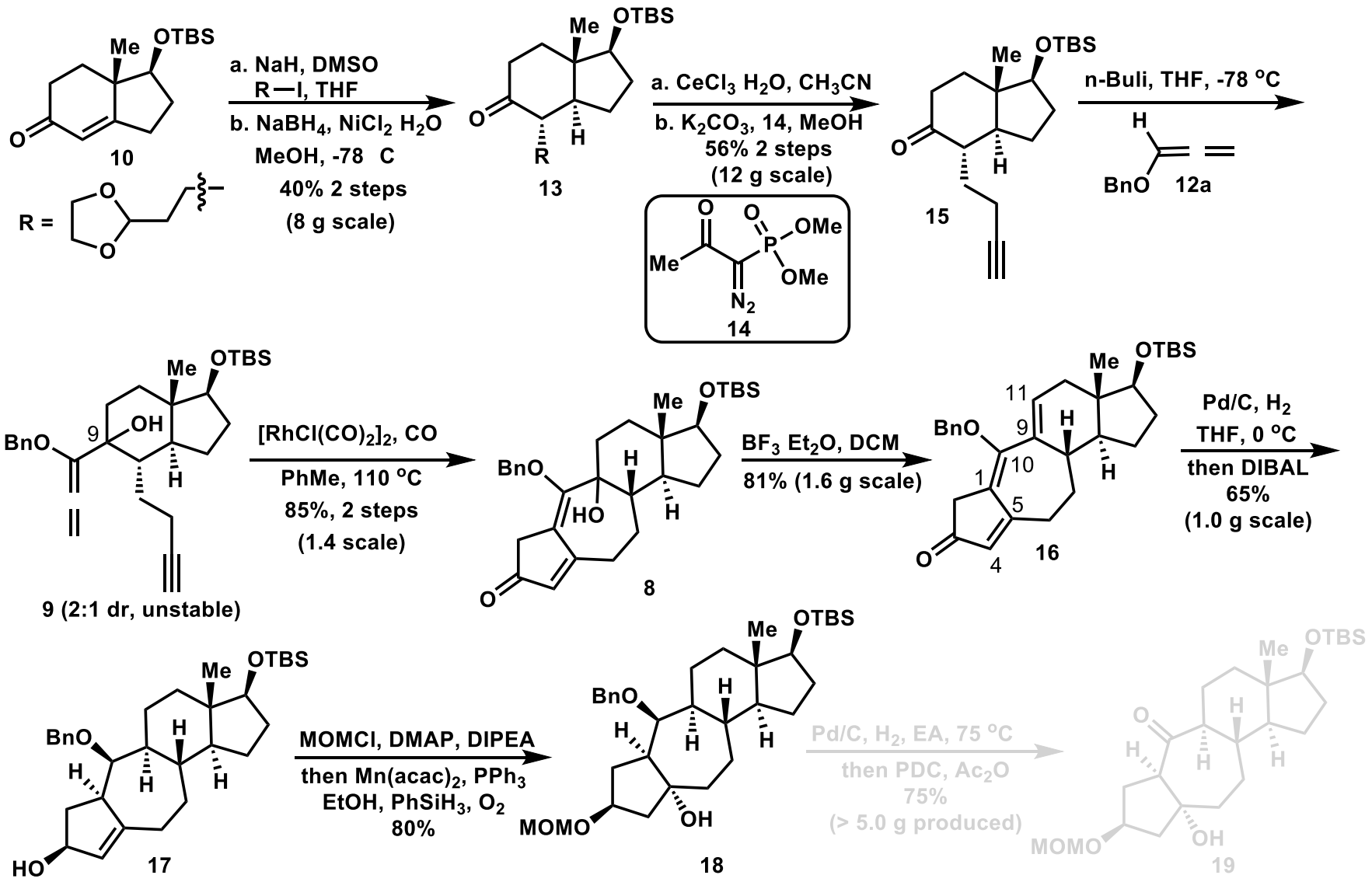

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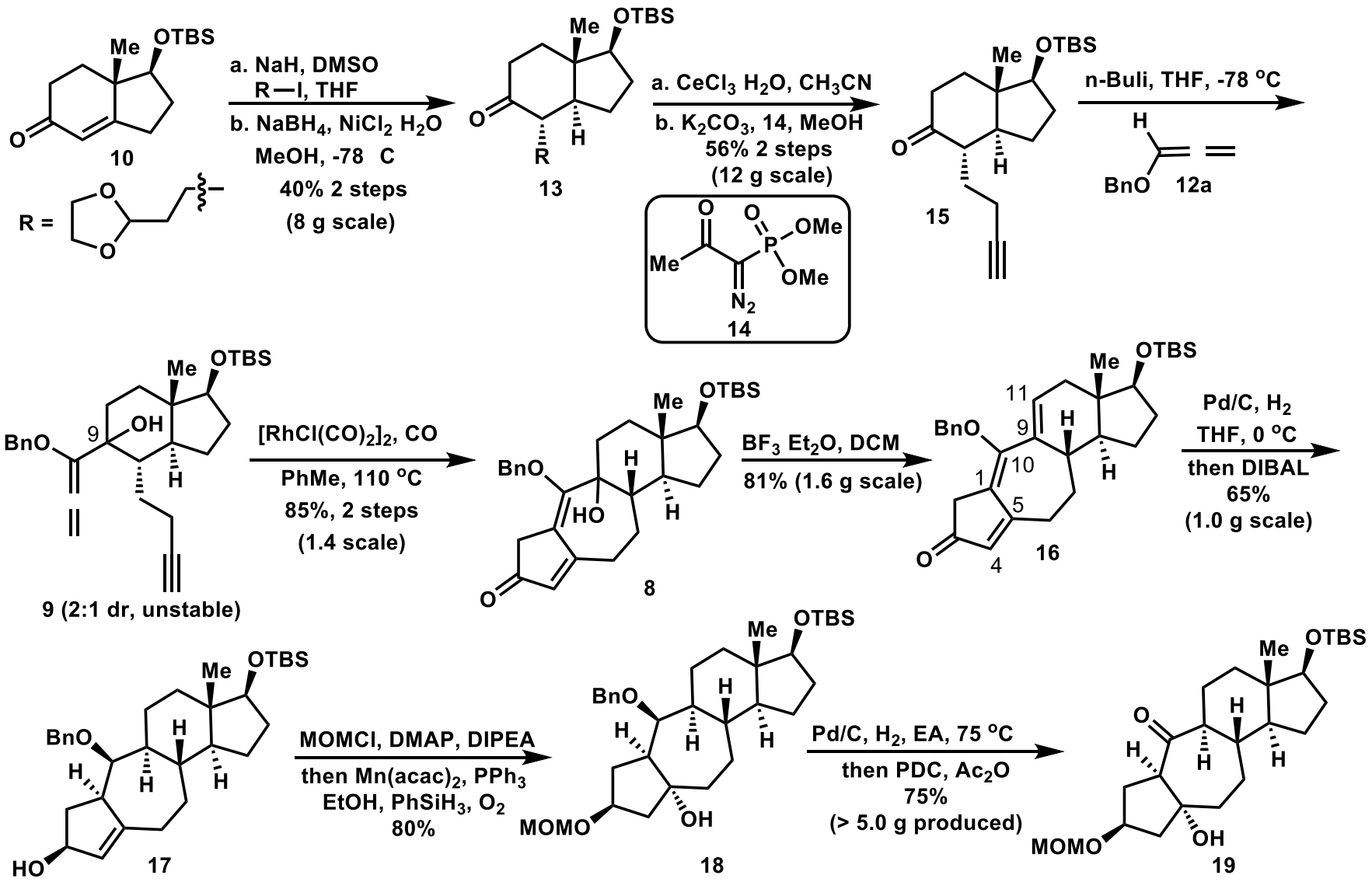
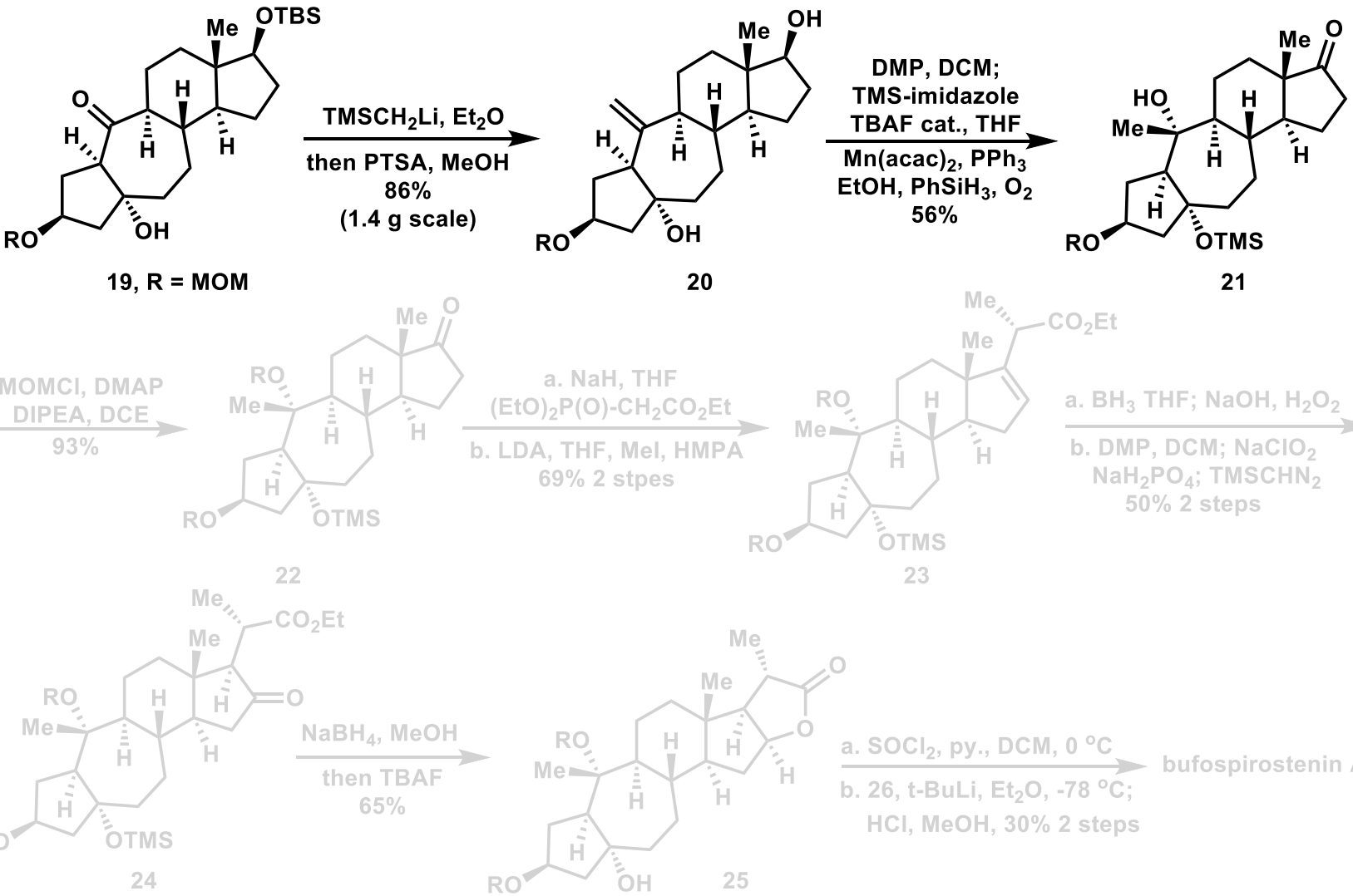


Total Synthesis of Bufospirostenin A



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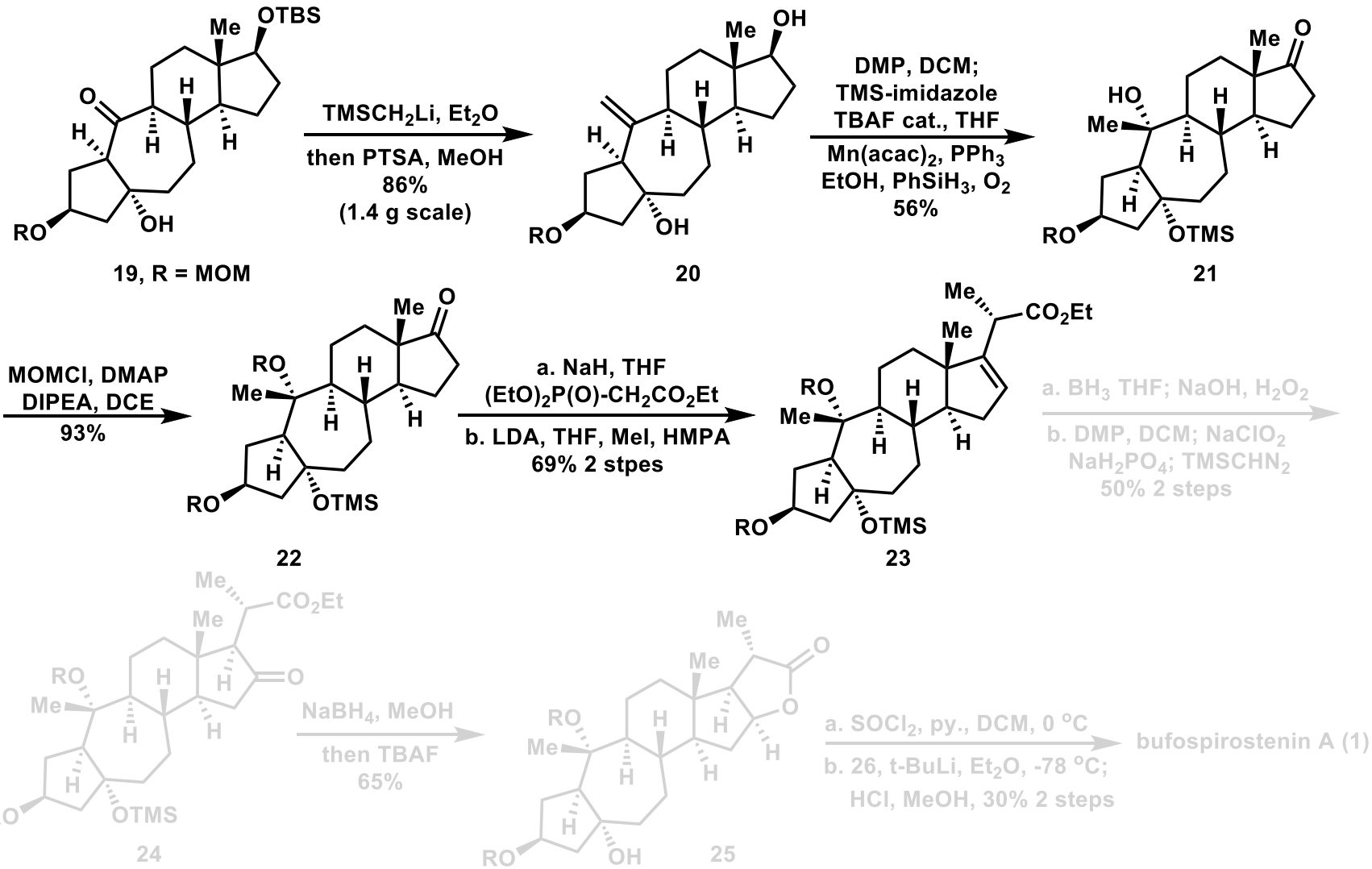

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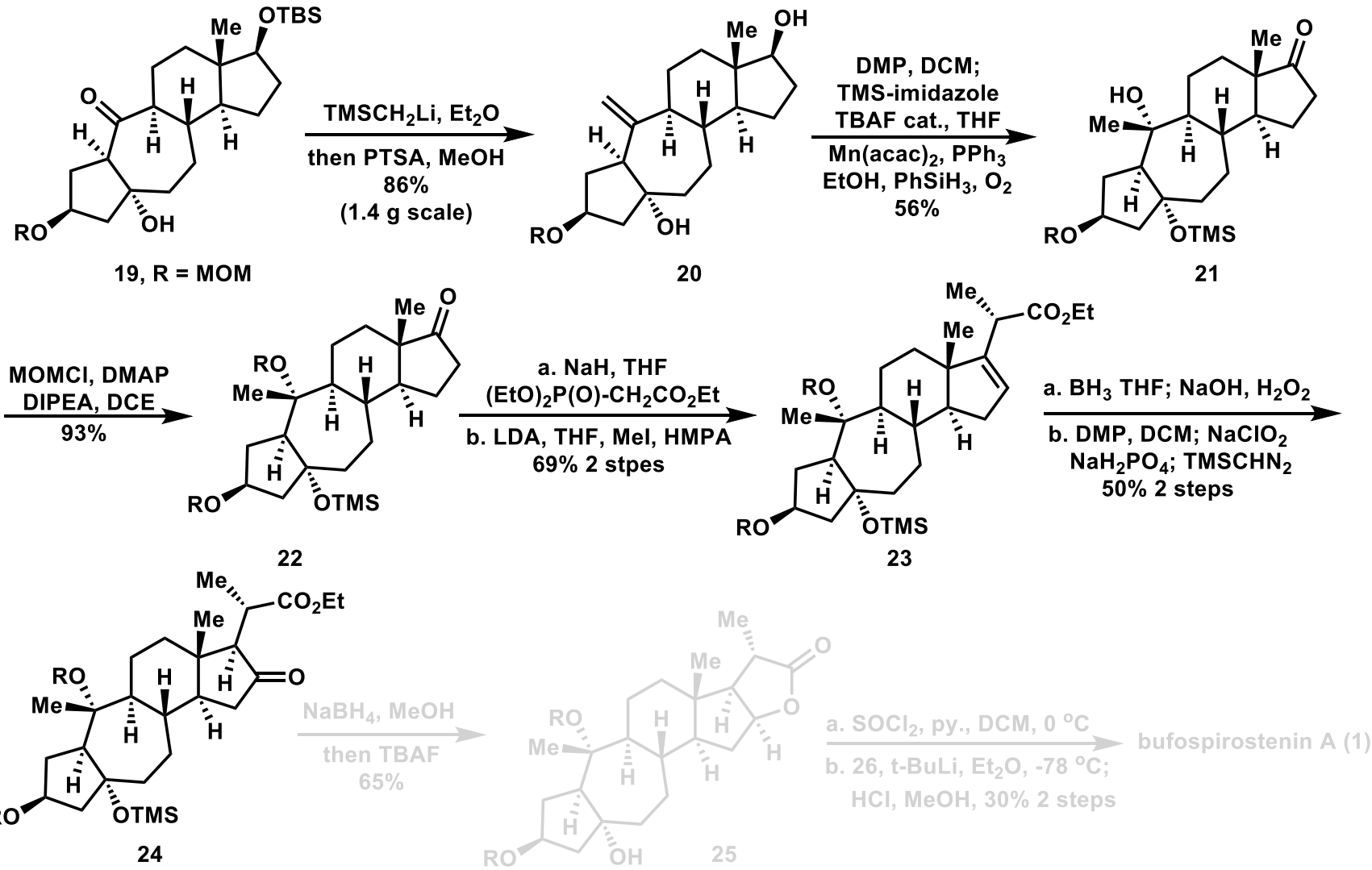

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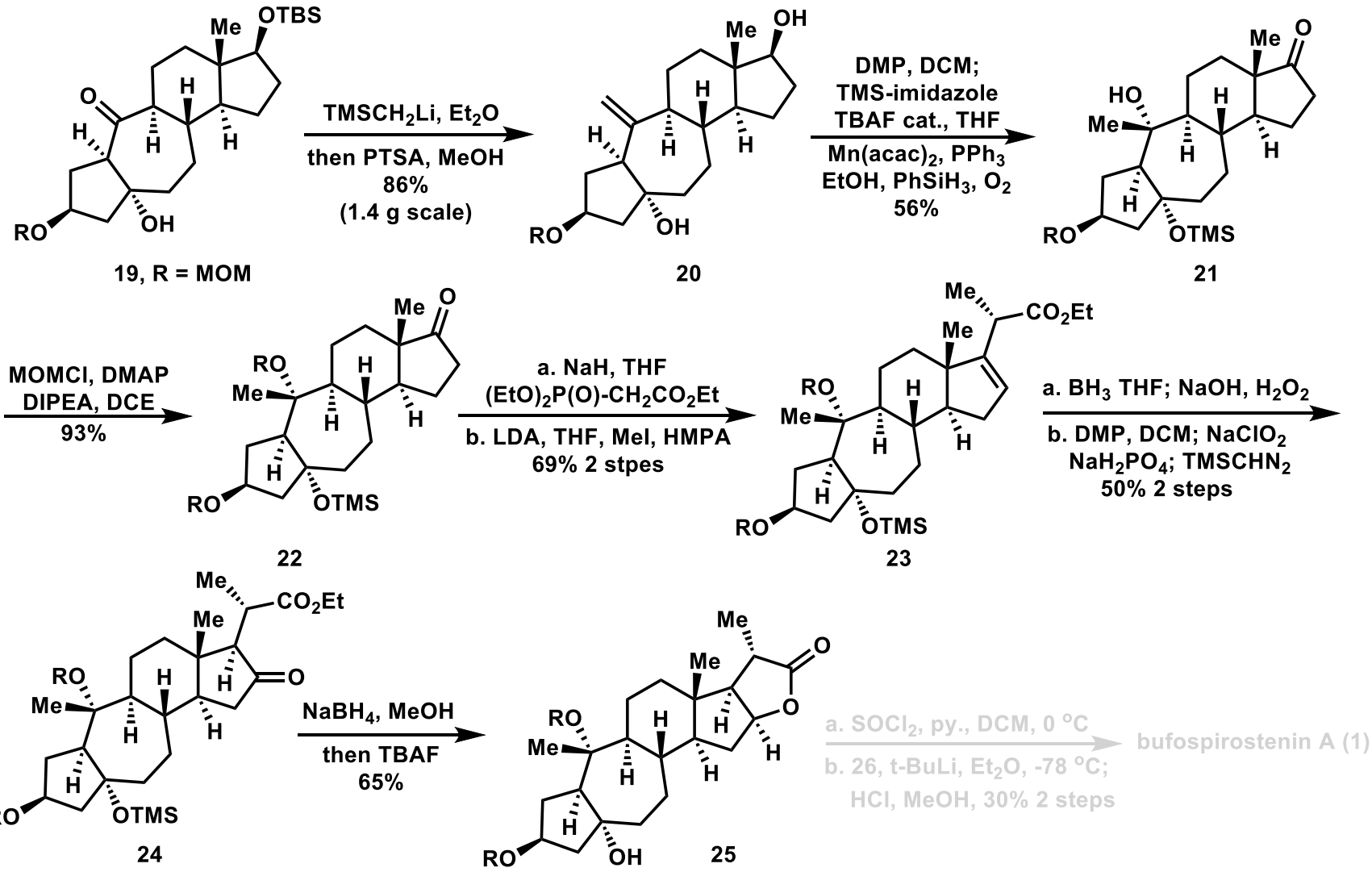

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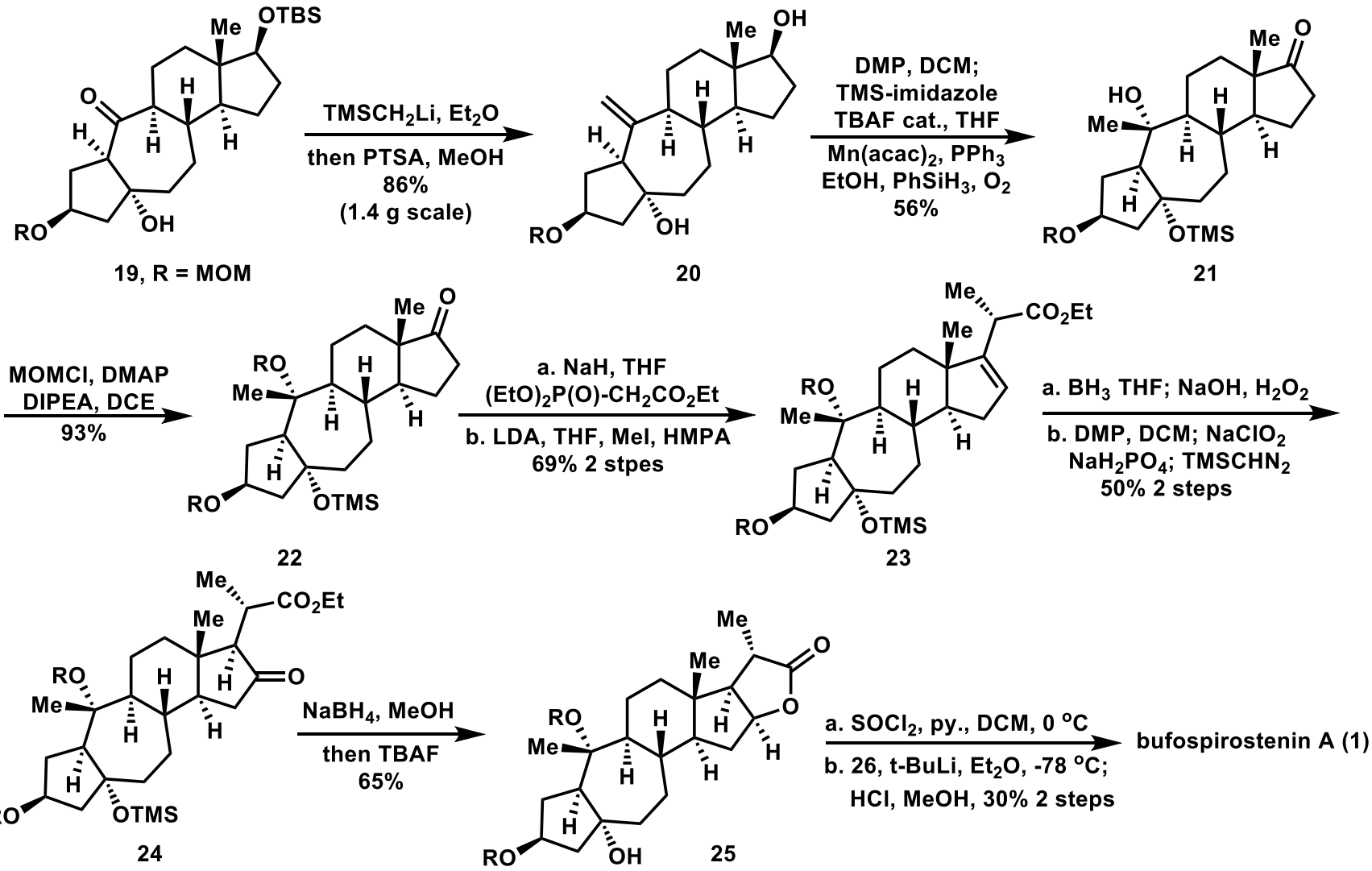
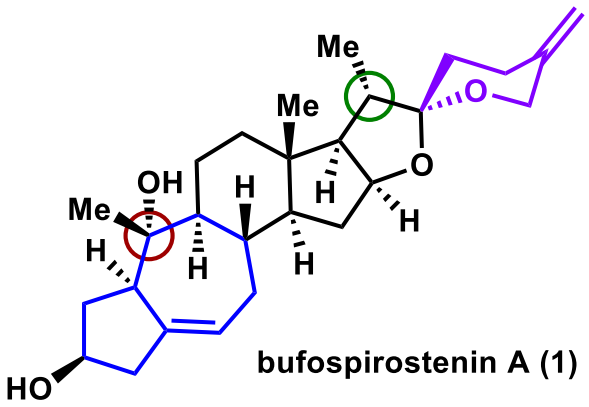


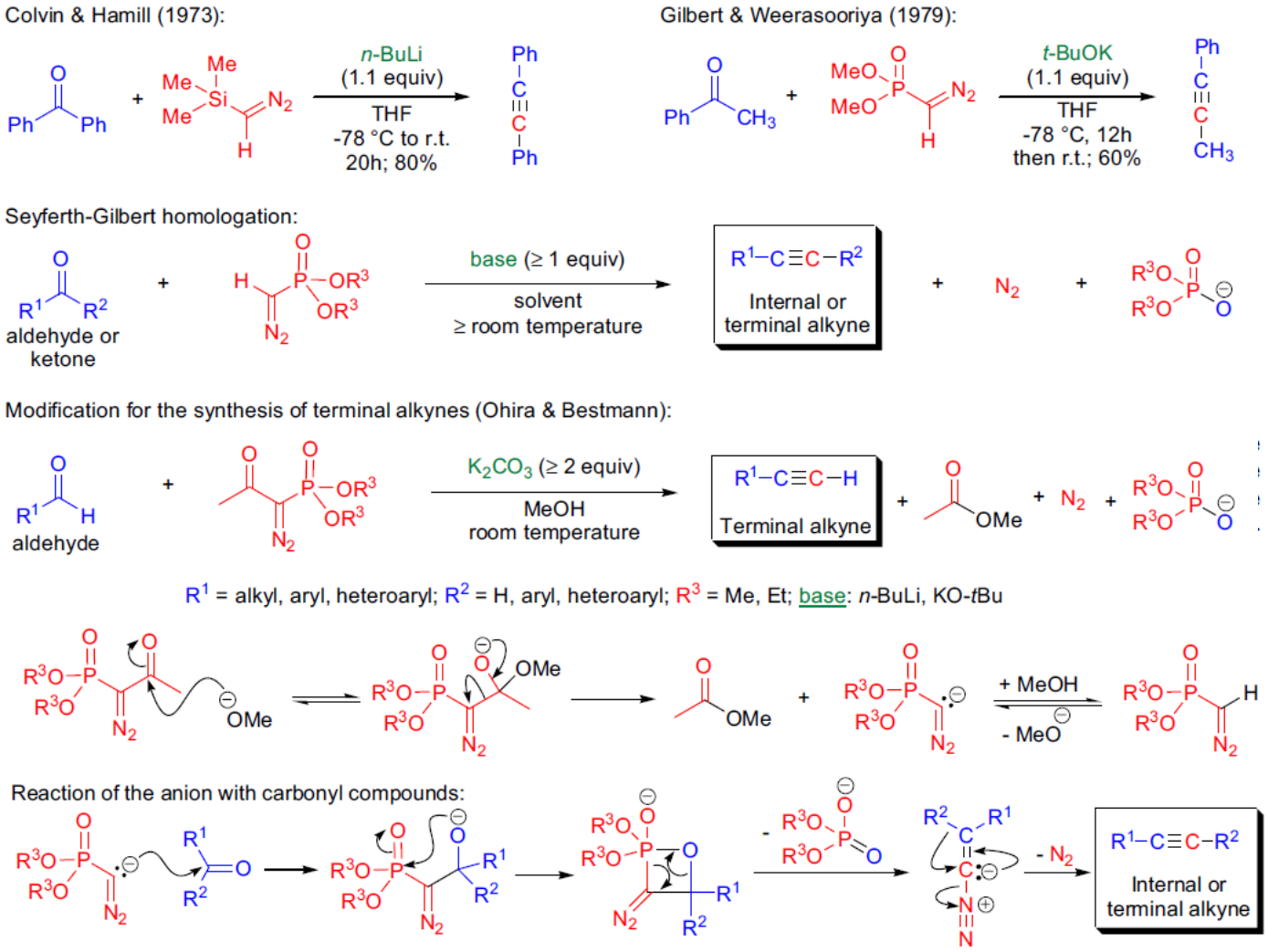


bufospirostenin A (1)

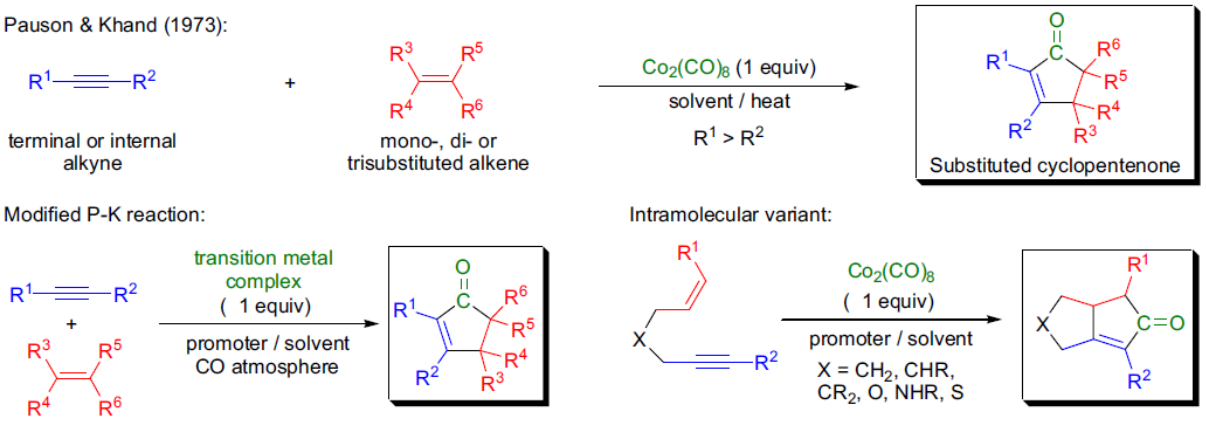
Mukaiyama hydration
Methylation
Pauson-Khand reaction of an alkoxyallene-yne
spiroketalization


PEKING UNIVERSITY
1898

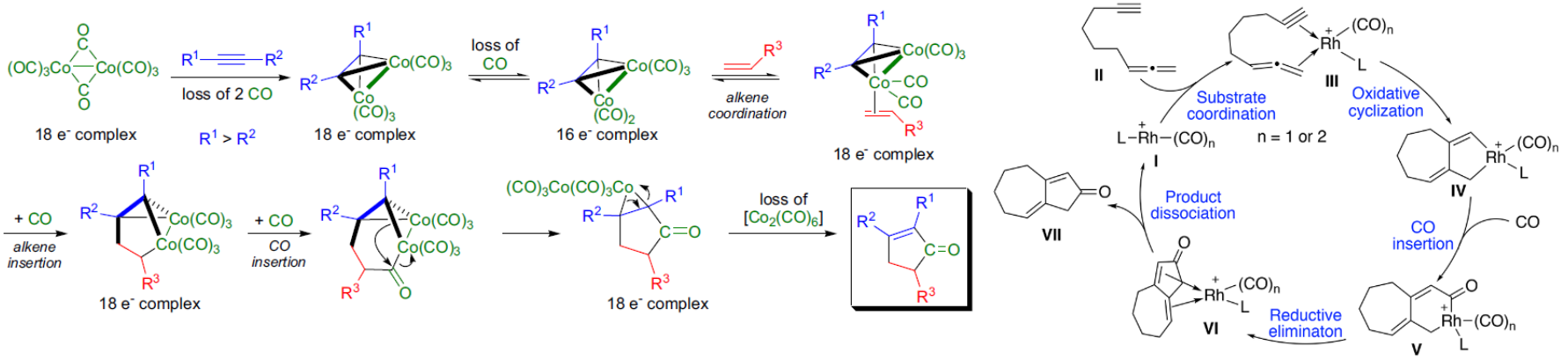
Seyferth-Gilbert homologation



Pauson–Khand reaction

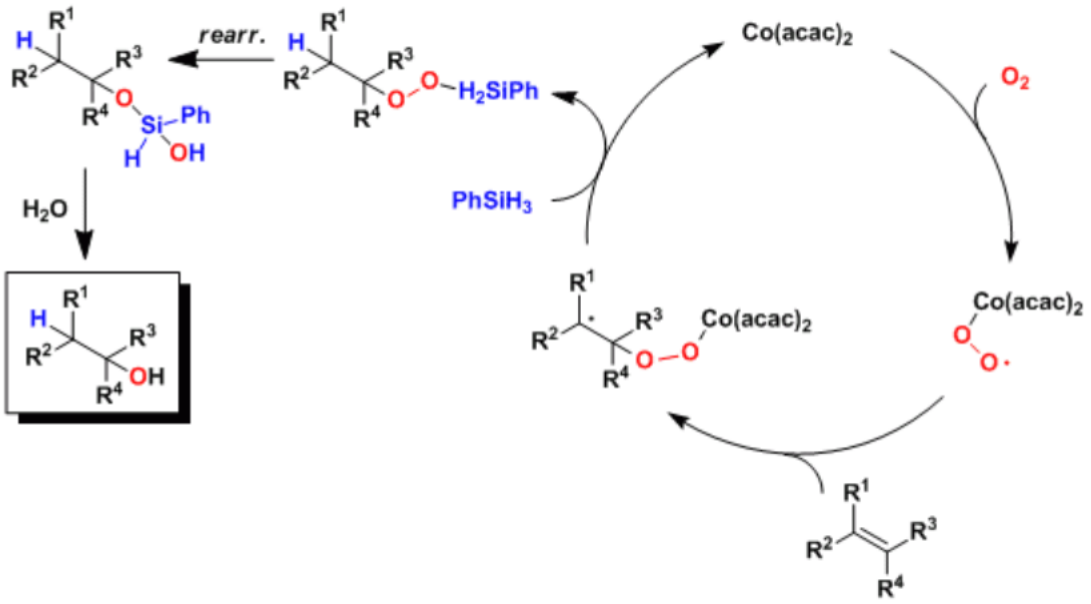


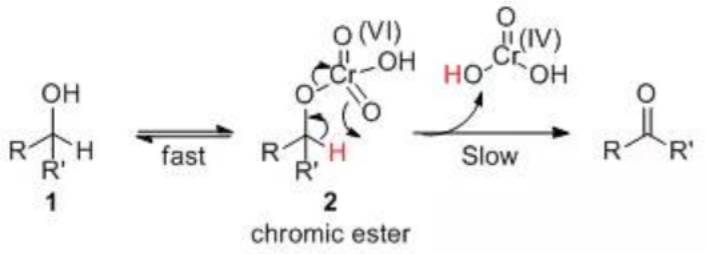
$R^{1\text{-}6}$ = H, alkyl, aryl, substituted alkyl and aryl; transition metal complex: $Co_2(CO)_8$, $Fe(CO)_5$, $Ru_2(CO)_{12}$, Cp_2TiR_2, $Ni(COD)_2$, $W(CO)_6$, $Mo(CO)_6$, $[RhCl(CO)_2]_2$; promoter: NMO, TMAO, $RSCH_3$, high-intensity light/photolysis, "hard" Lewis base



Mukaiyama hydration

- Reaction Mechanism




OH
R
H
R'
1
fast
O (VI)
Cr
OH
O
O
R
H
R'
2
chromic ester
O
(IV)
HO
Cr
OH
Slow
O
R
R'

Horner-Wadsworth-Emmons olefination