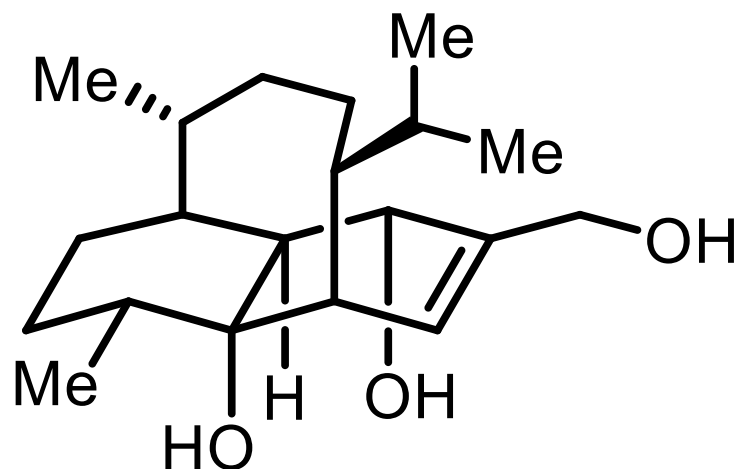


Vinigrol

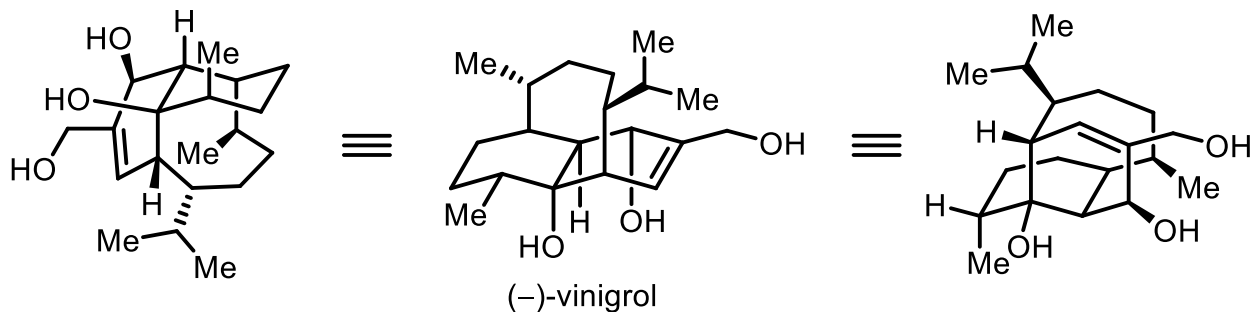


Matt Nelli

Synthesis Club

25 November 2019

Vinigrol Background



Virgaria nigra F-5408

Isolated and characterized: **1987**

Activity:

- Antihypertensive
- Inhibits PAF-induced platelet aggregation in human plasma @ $IC_{50} = 33$ nM (PAF = platelet activating factor)
- TNF (tumor necrosis factor) antagonist; TNF involved in human inflammation process

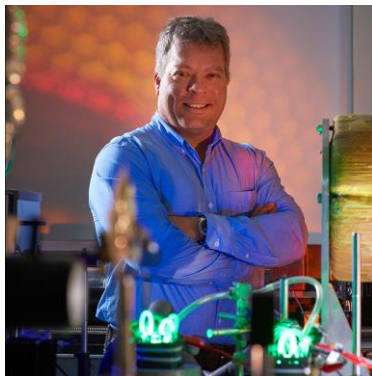
Chemical Interest:

- Before first total synthesis (**2008**): 17 publications (including Corey, Paquette, Barriault) & 4 PhD dissertations
- Challenging diterpene system: 8-contiguous stereocenters, compact caged structure

Synthetic History



Phil Baran, Scripps Research Inst.
2008 – *Total Synthesis*



Louis Barriault, Univ. of Ottawa
2012 – *Formal Synthesis*



Jon Njardarson, Univ. of Arizona
2013 – *Total Synthesis*



Krishna Kaliappan, Indian Inst. Tech.
Bombay
2014 – *Formal Synthesis*



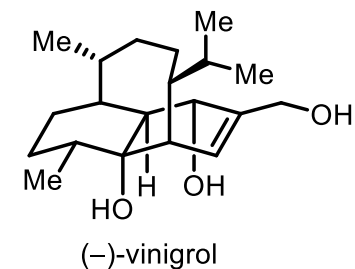
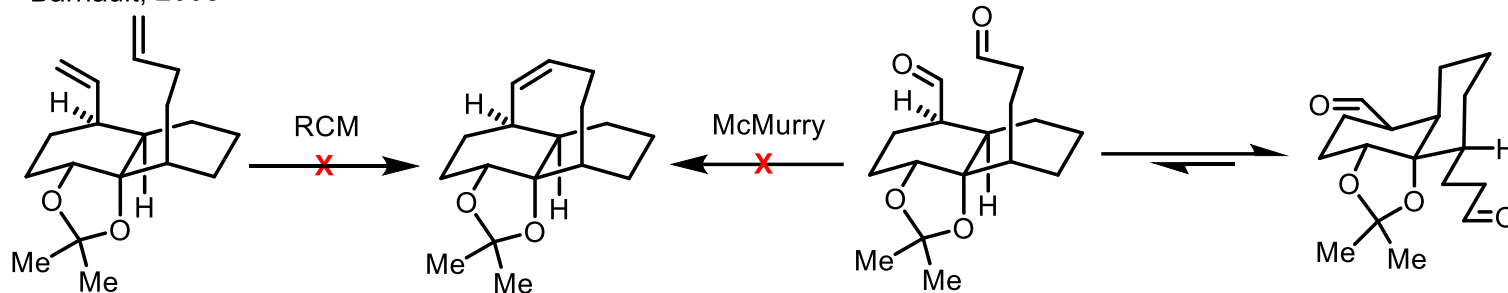
Tuoping Luo,
Peking Univ.
Feb. 2019 – *Total Synthesis*



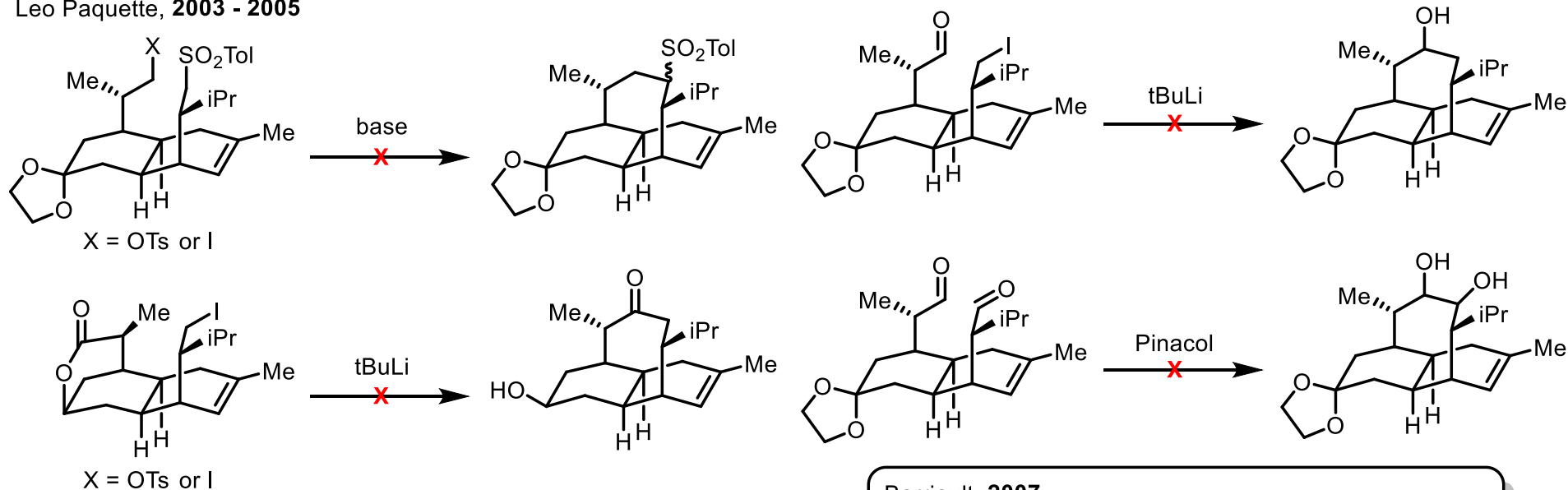
Chuang-Chuang Li,
Shenzen Grubbs Inst. - Southern
Univ. Sci. & Tech.
Sept. 2019 – *Total Synthesis*

Brief Overview of Synthetic Attempts

Barriault, 2005



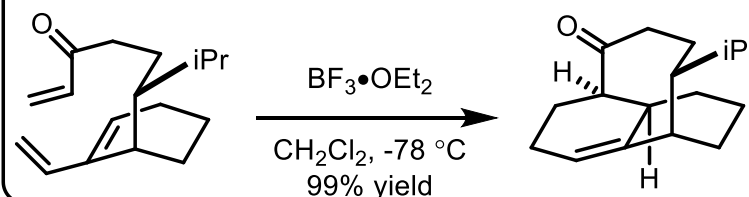
Leo Paquette, 2003 - 2005



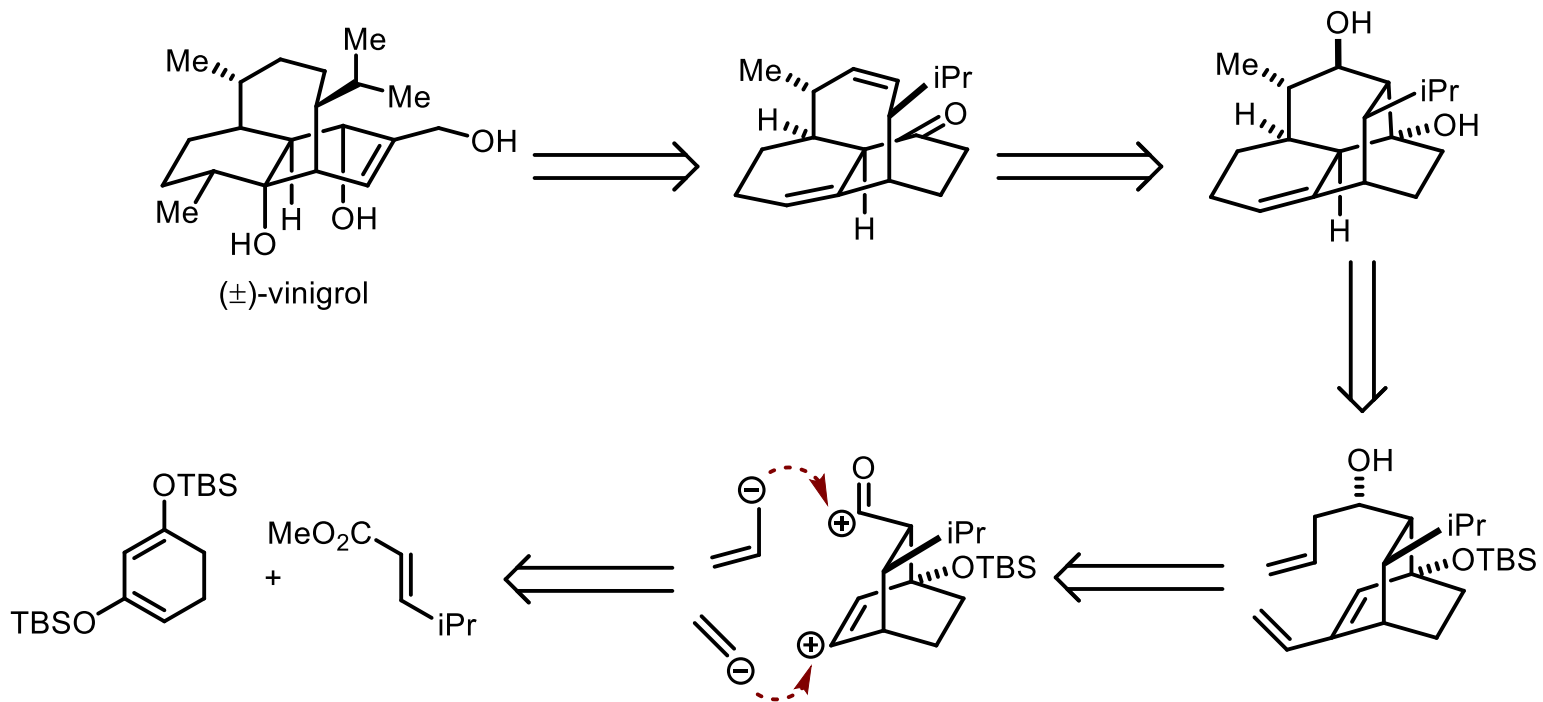
Other Strategies:

- RCM (decalin and cyclohexane)
- ring contraction (e.g. Ramberg-Bäcklund)

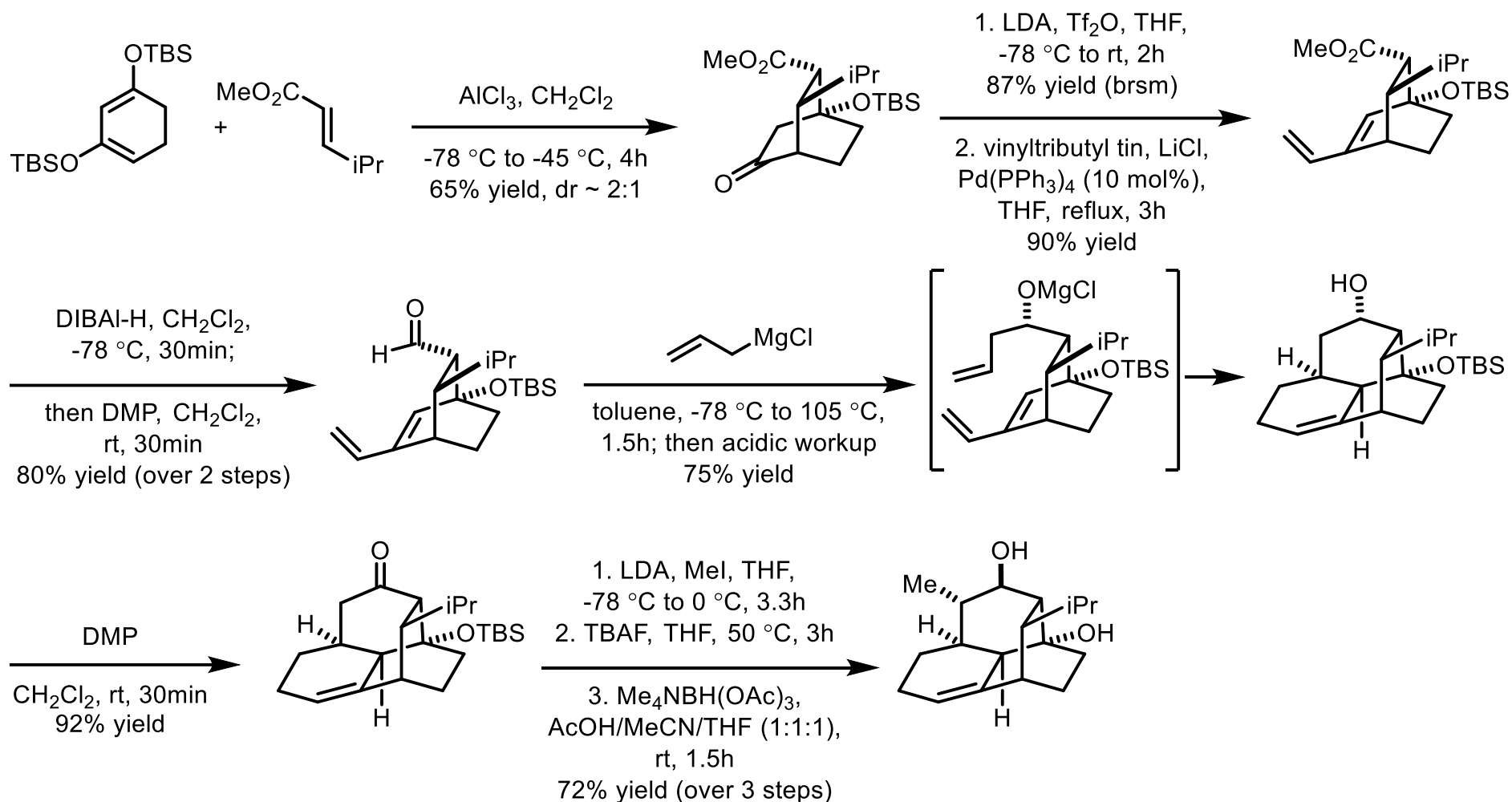
Barriault, 2007



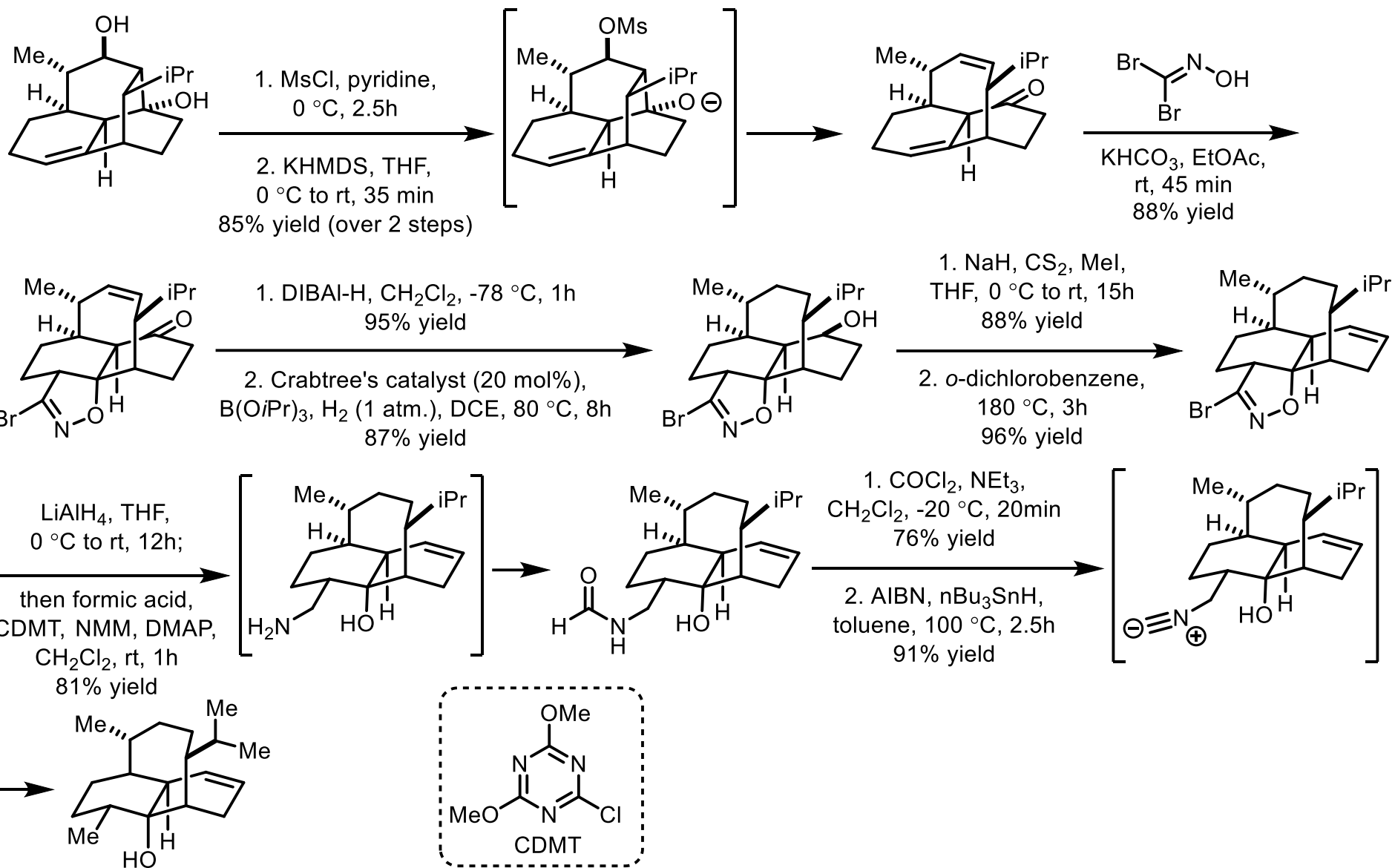
Baran's Synthesis of (±)-Vinigrol (2009)



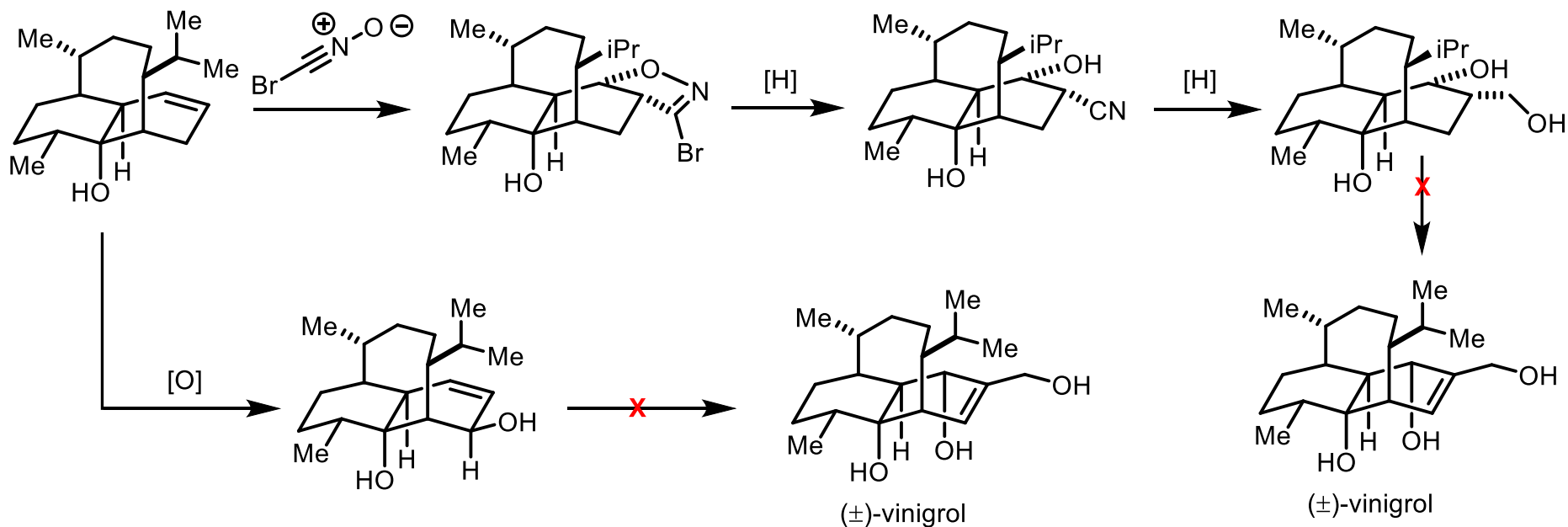
Baran's Synthesis of (±)-Vinigrol (2009)



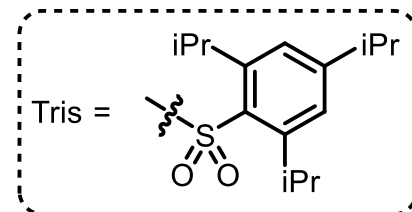
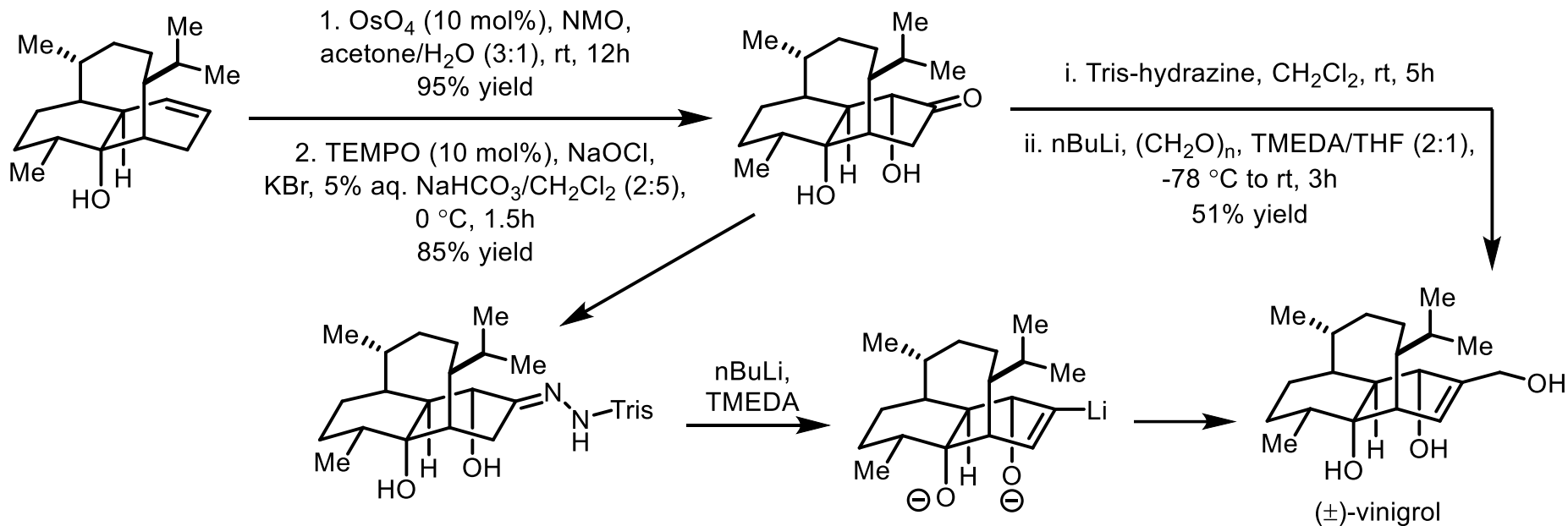
Baran's Synthesis of (±)-Vinigrol (2009)



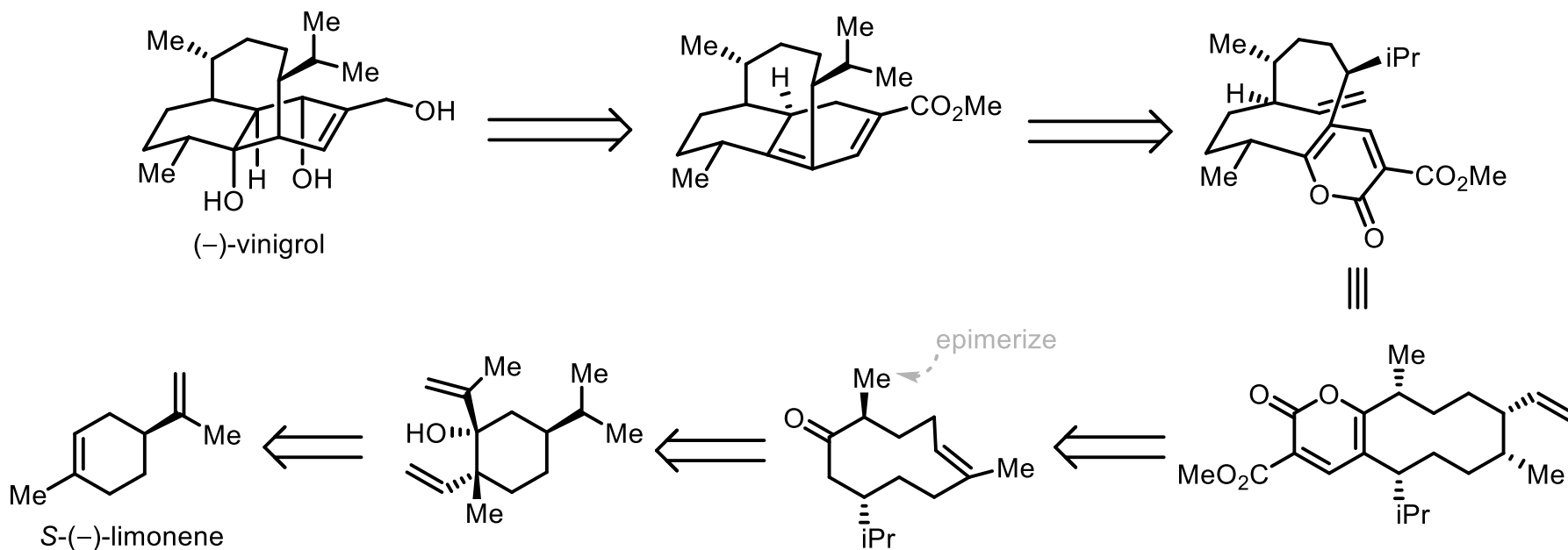
Baran's Synthesis of ($\pm$)-Vinigrol (2009)



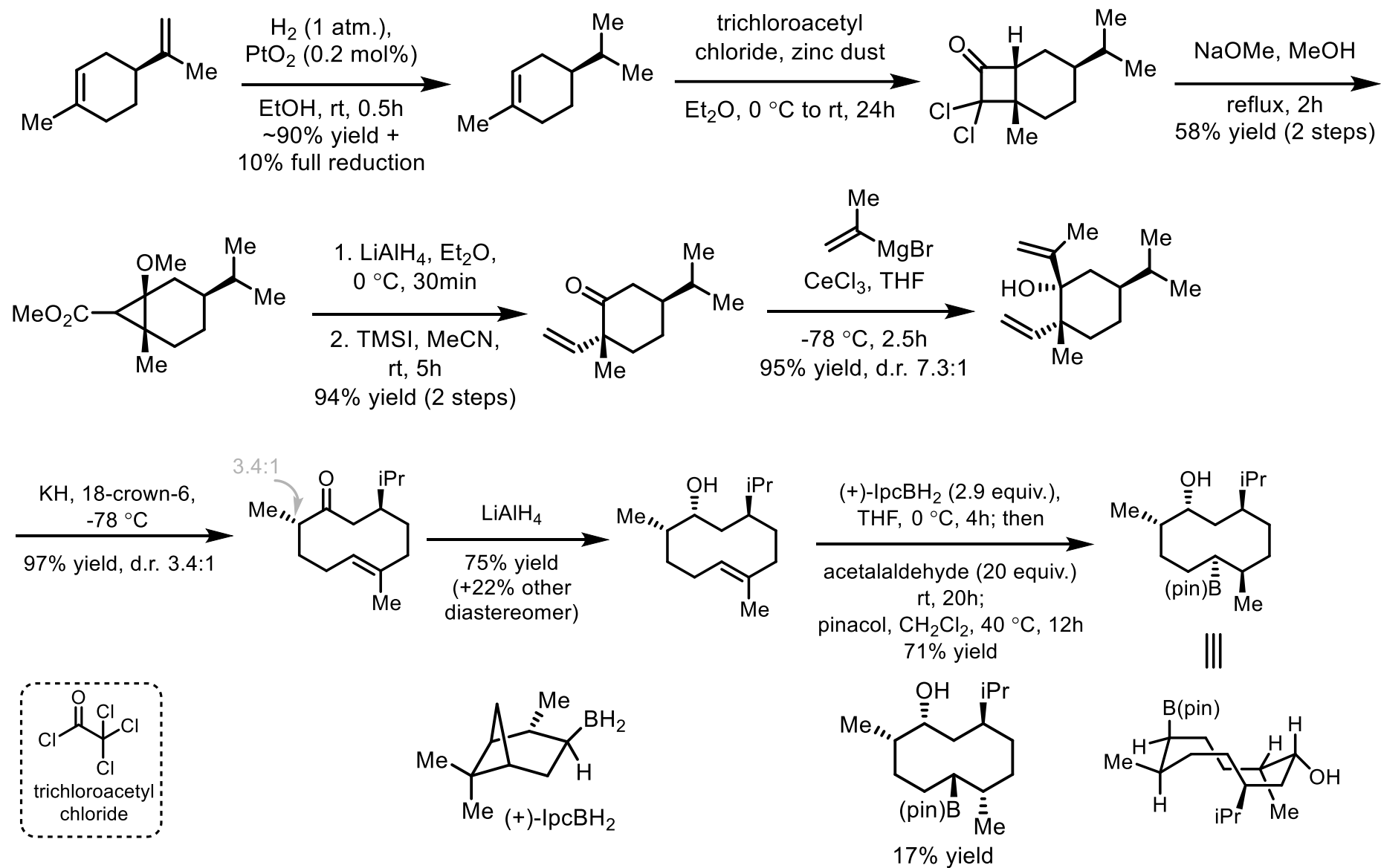
Baran's Synthesis of (±)-Vinigrol (2009)



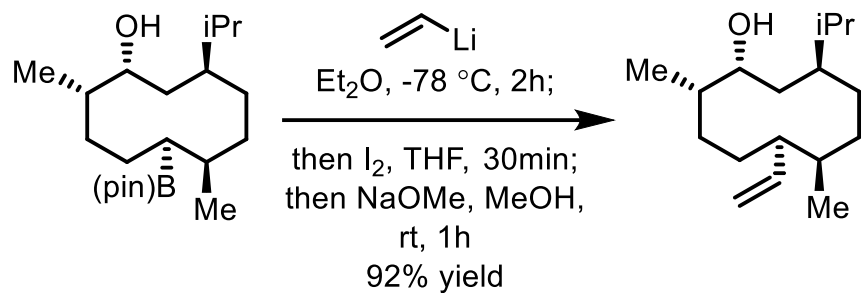
Luo's Synthesis of (–)-Vinigrol (2019)



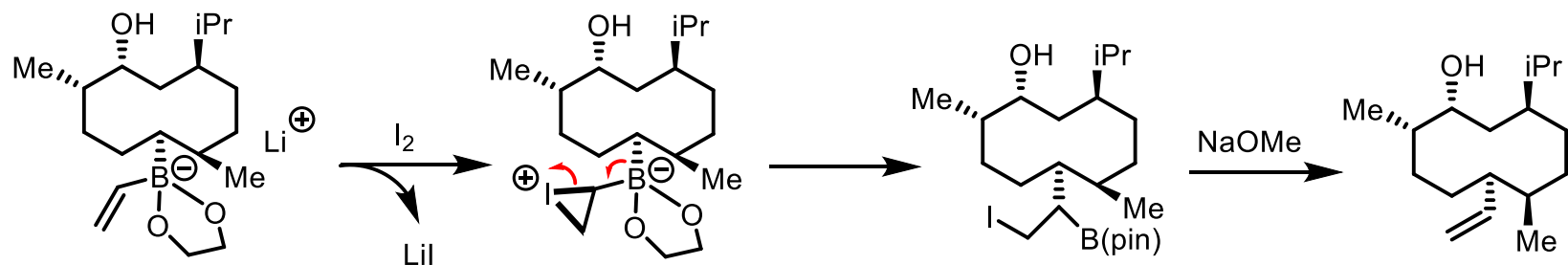
Luo's Synthesis of (–)-Vinigrol (2019)



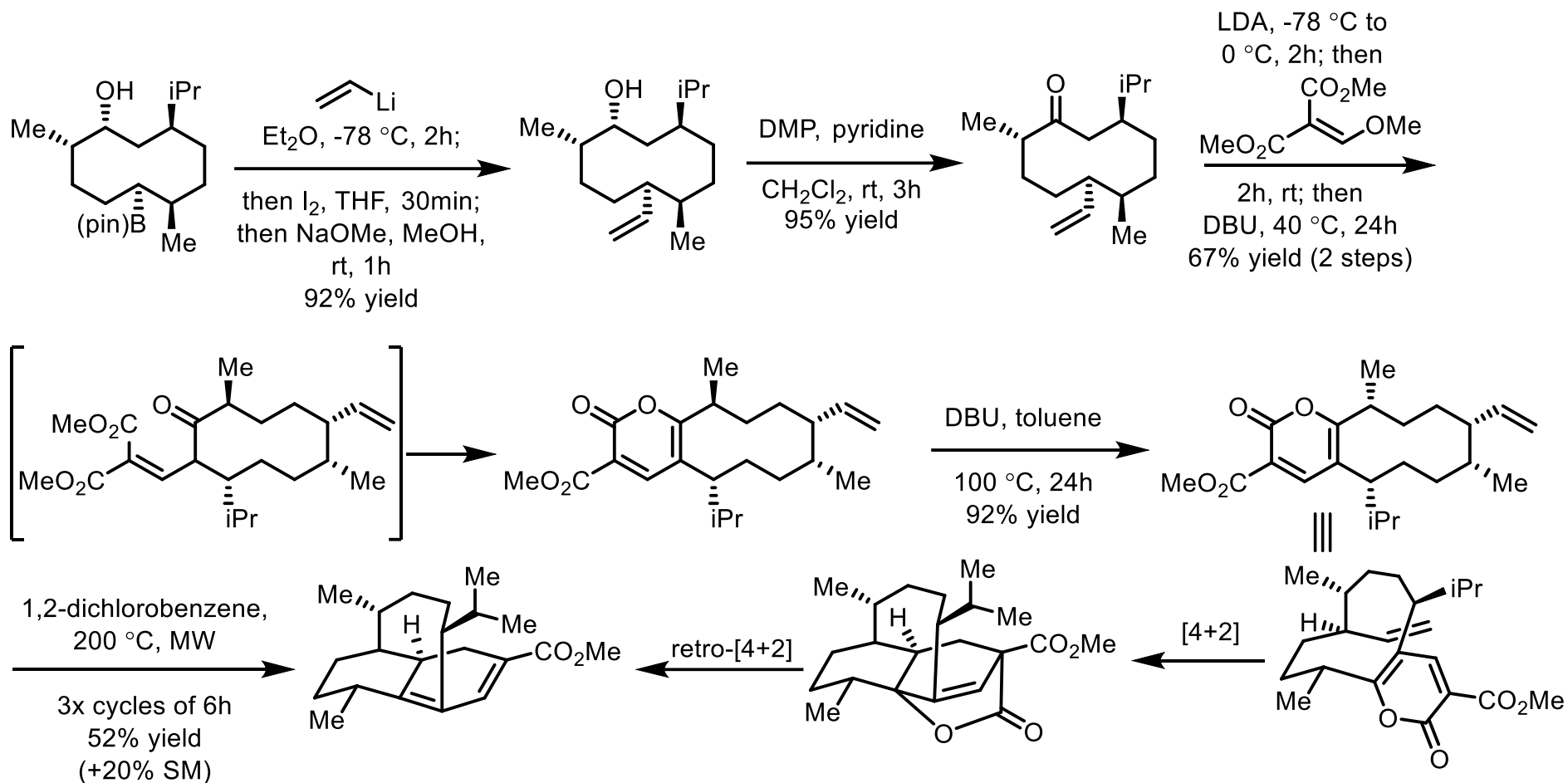
Luo's Synthesis of (–)-Vinigrol (2019)



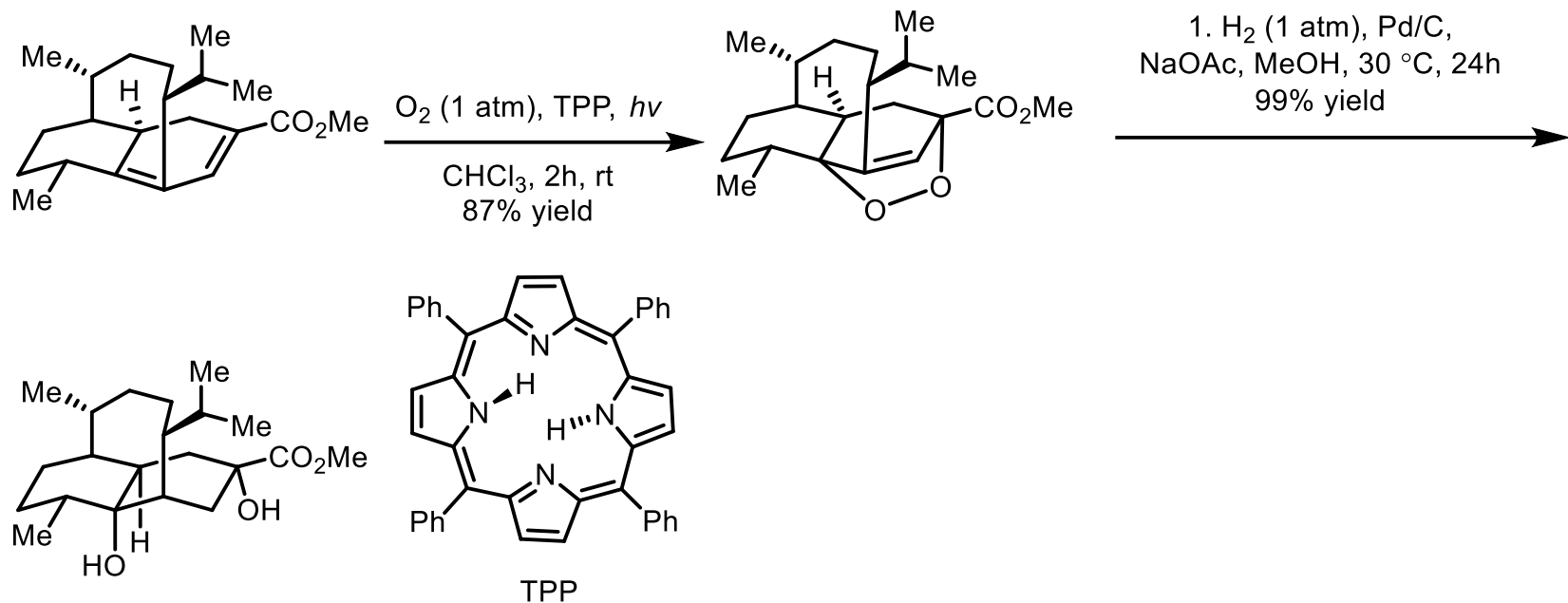
Zweifel olefination



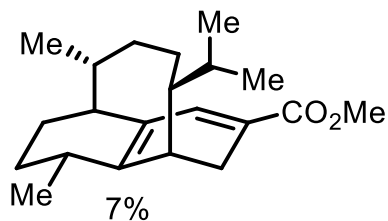
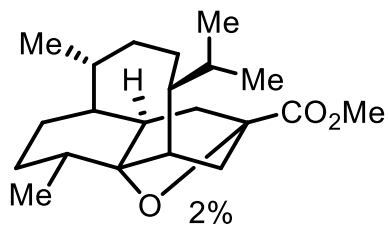
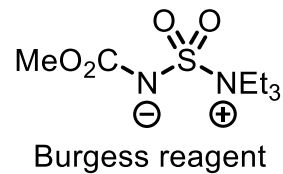
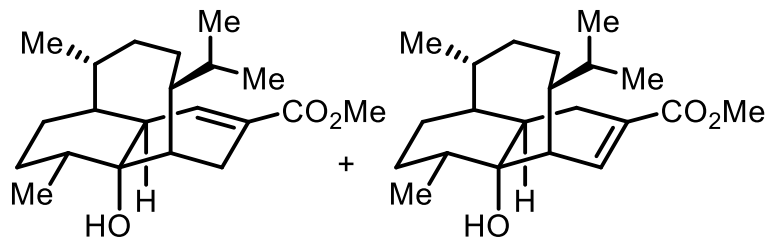
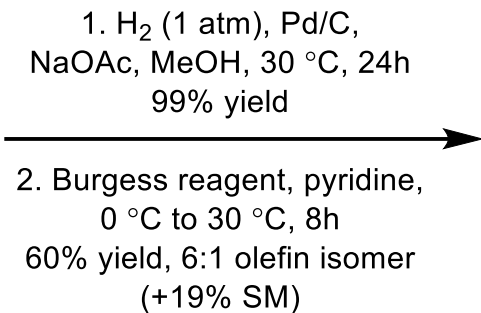
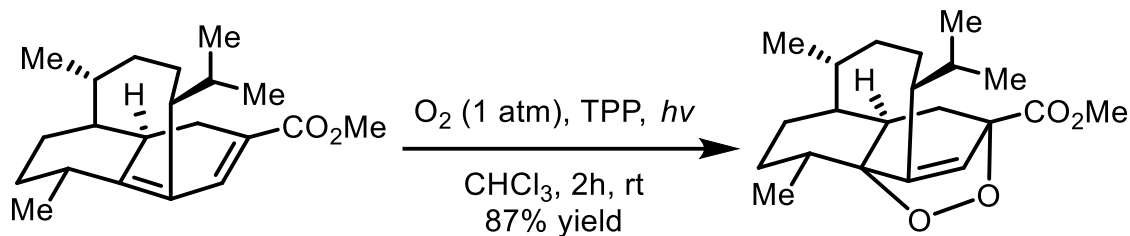
Luo's Synthesis of (–)-Vinigrol (2019)



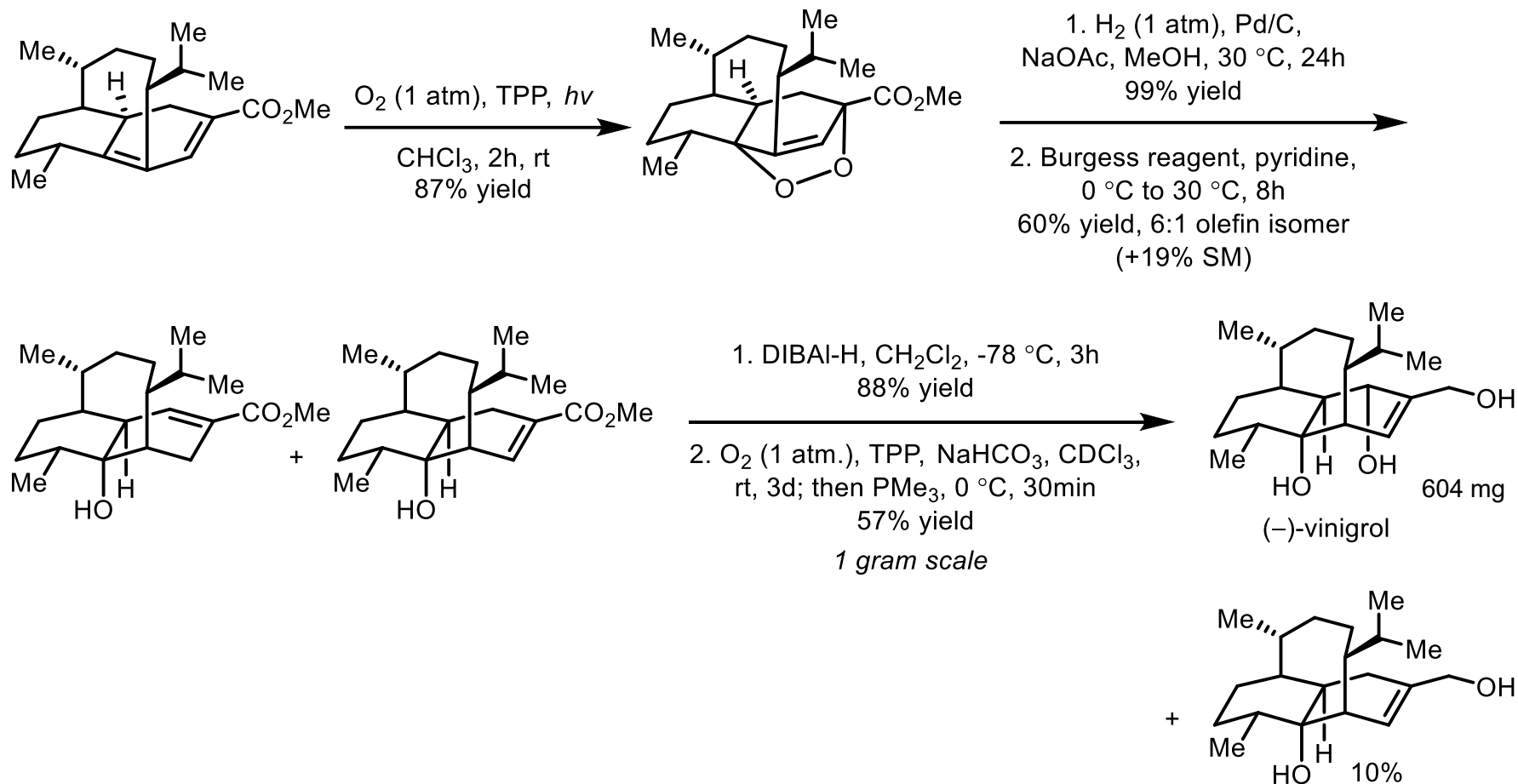
Luo's Synthesis of (–)-Vinigrol (2019)



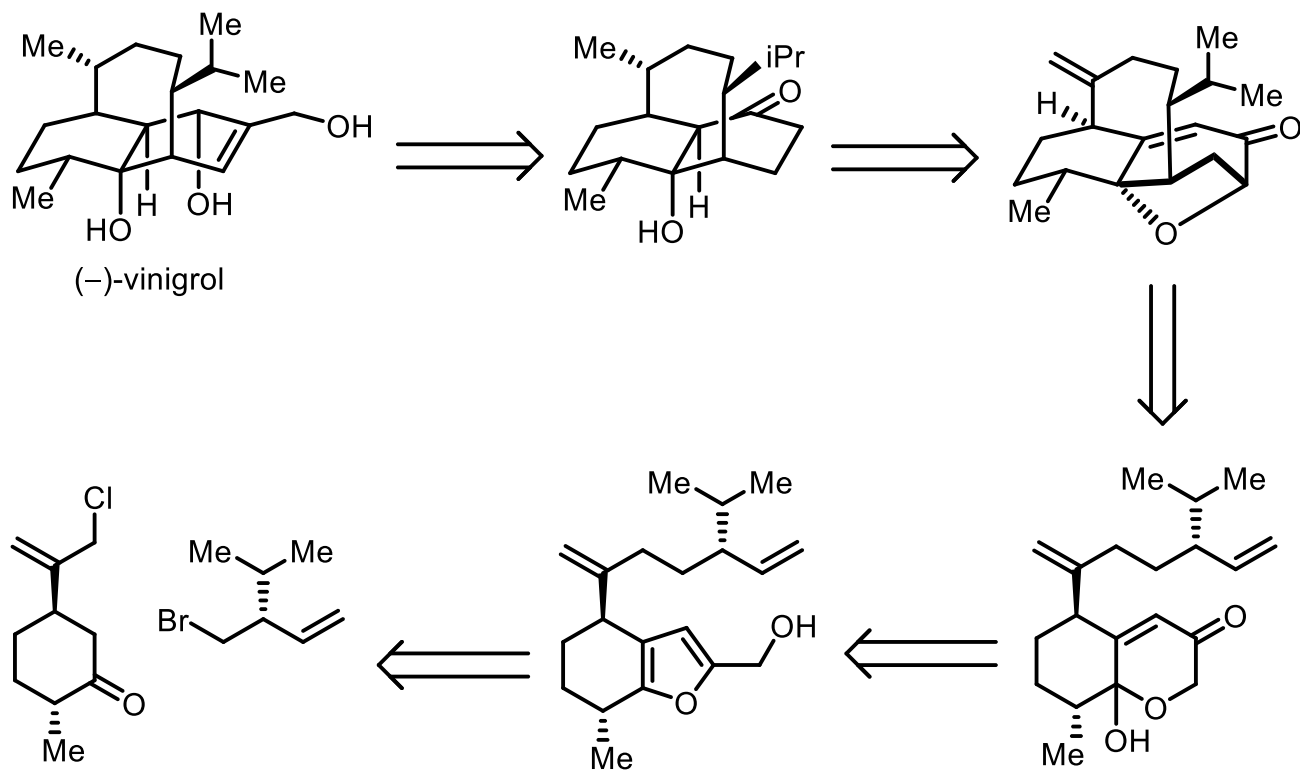
Luo's Synthesis of (–)-Vinigrol (2019)



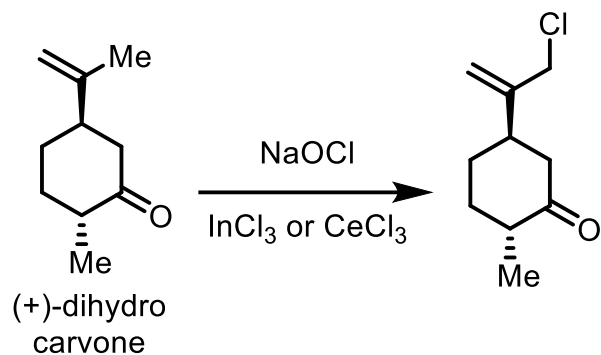
Luo's Synthesis of (–)-Vinigrol (2019)



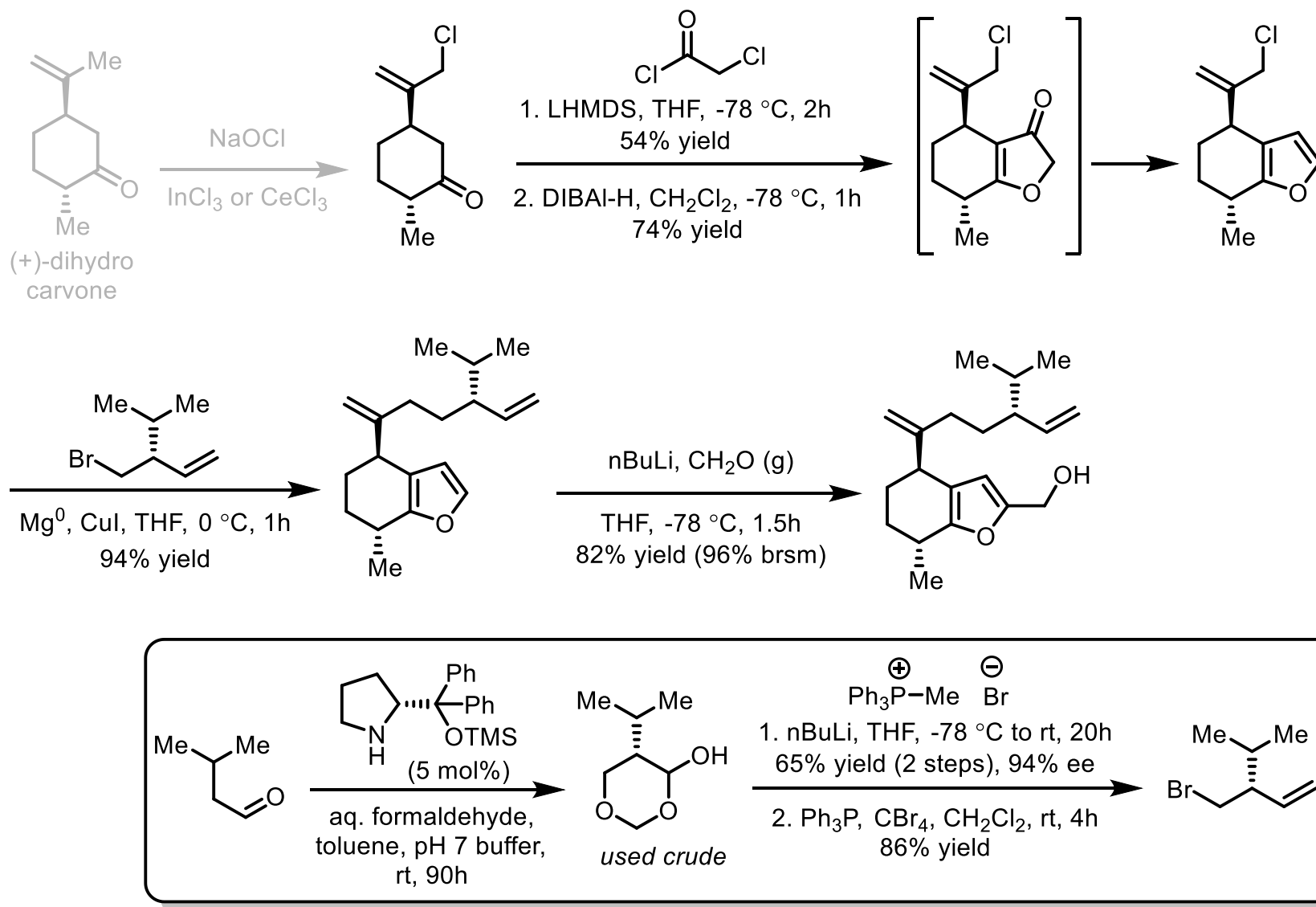
Li's Synthesis of (–)-Vinigrol (2019)



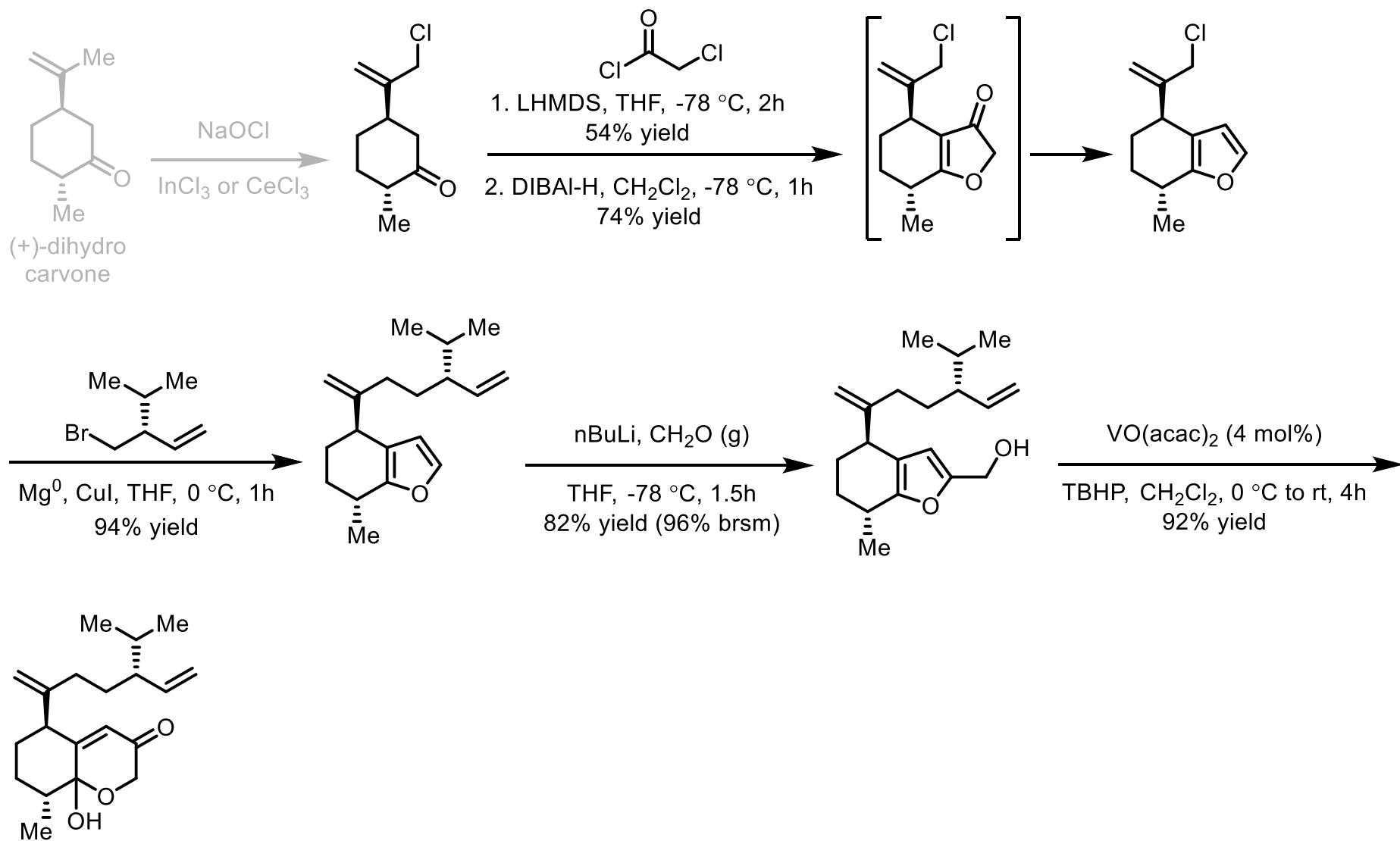
Li's Synthesis of (–)-Vinigrol (2019)



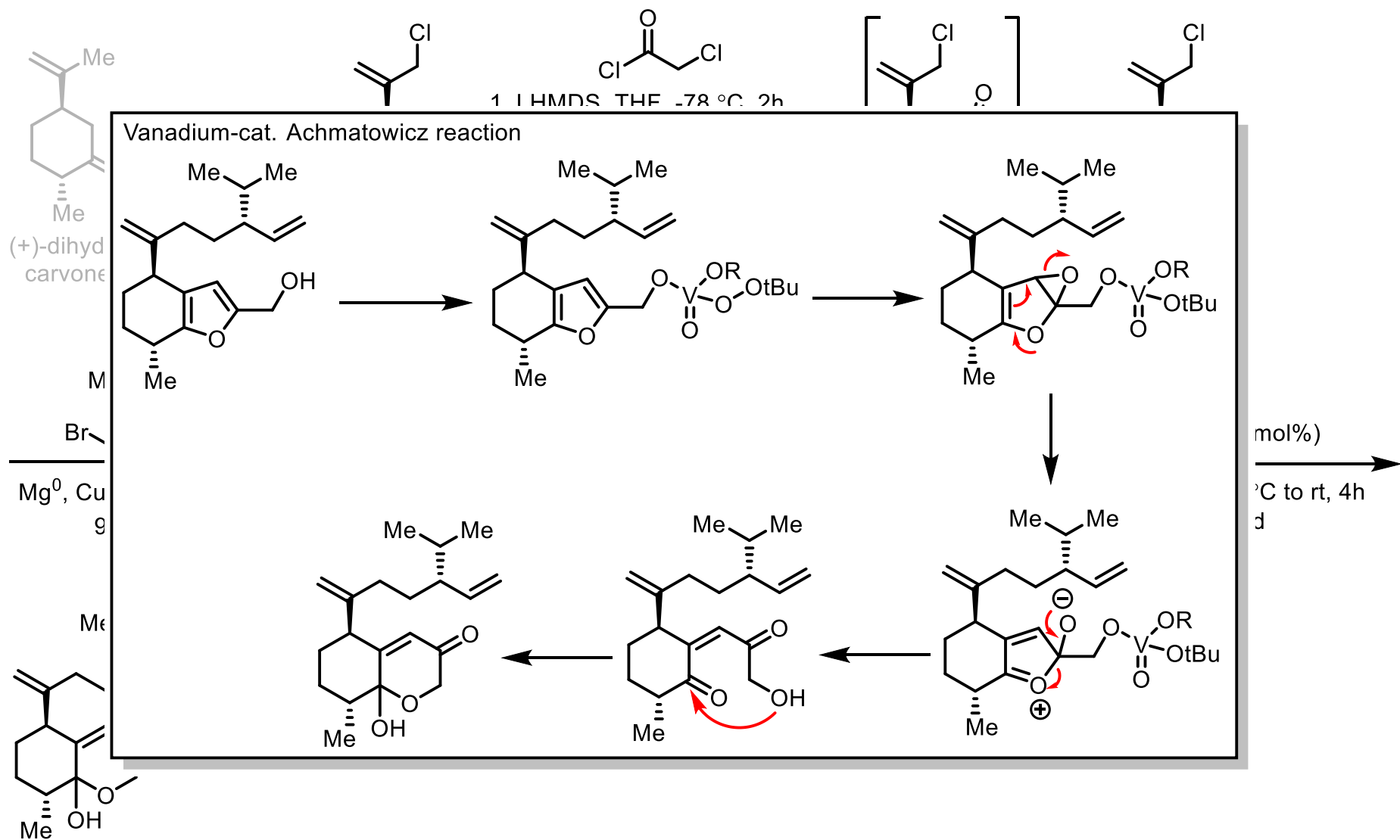
Li's Synthesis of (–)-Vinigrol (2019)



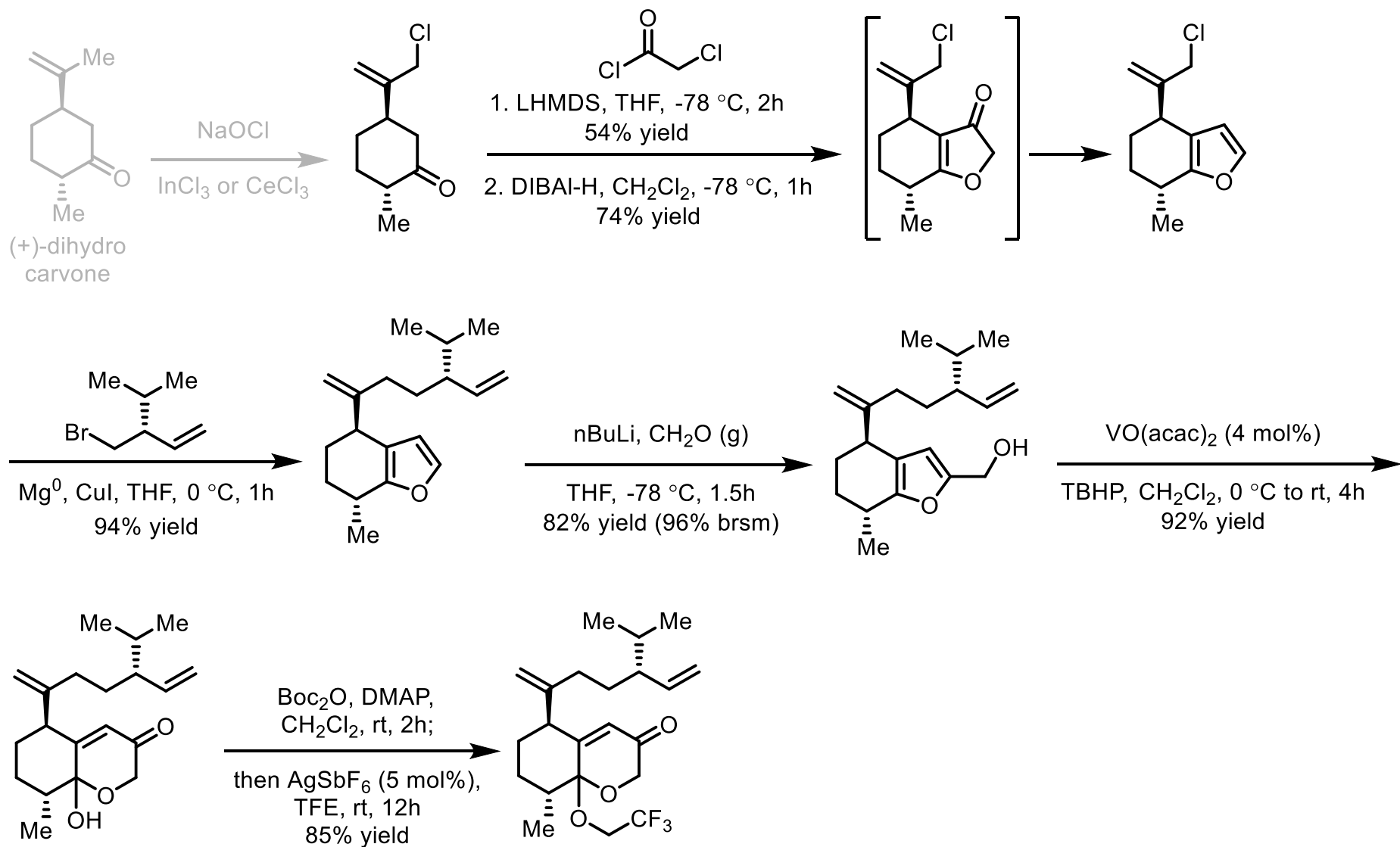
Li's Synthesis of (–)-Vinigrol (2019)



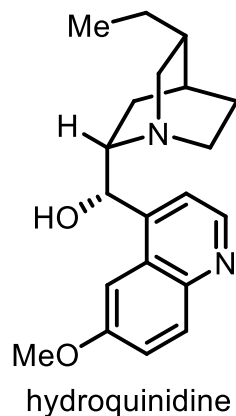
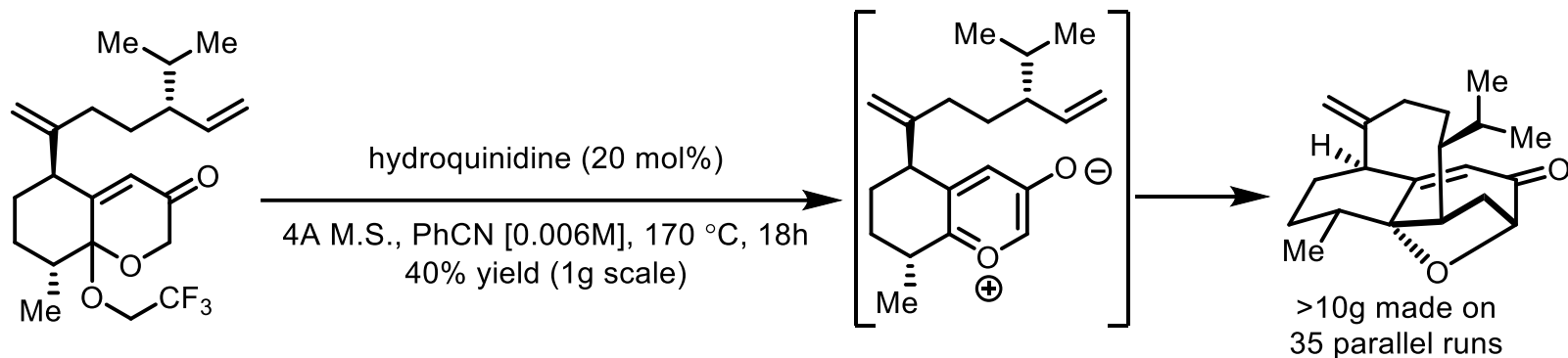
Li's Synthesis of (–)-Vinigrol (2019)



Li's Synthesis of (–)-Vinigrol (2019)

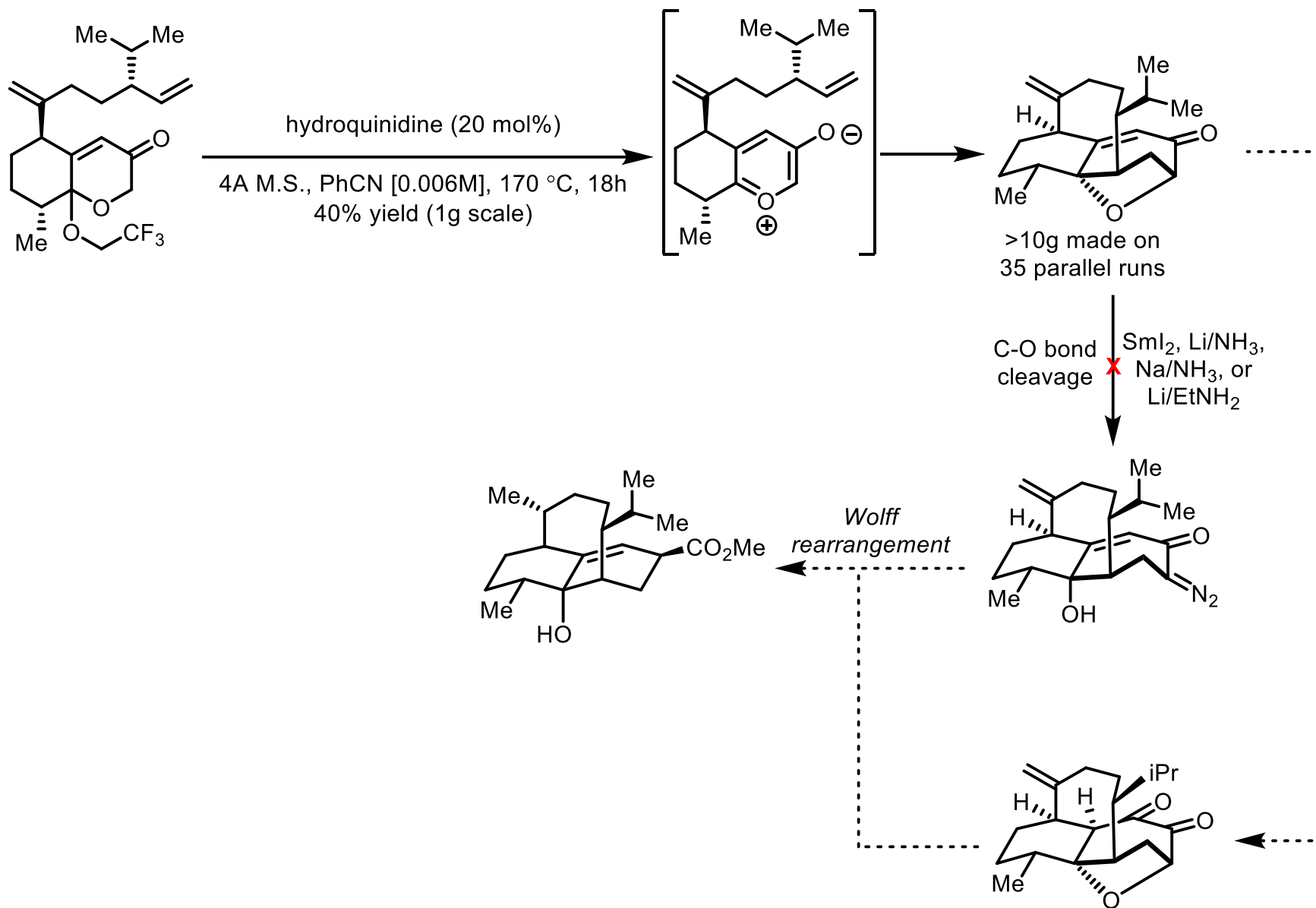


Li's Synthesis of (–)-Vinigrol (2019)

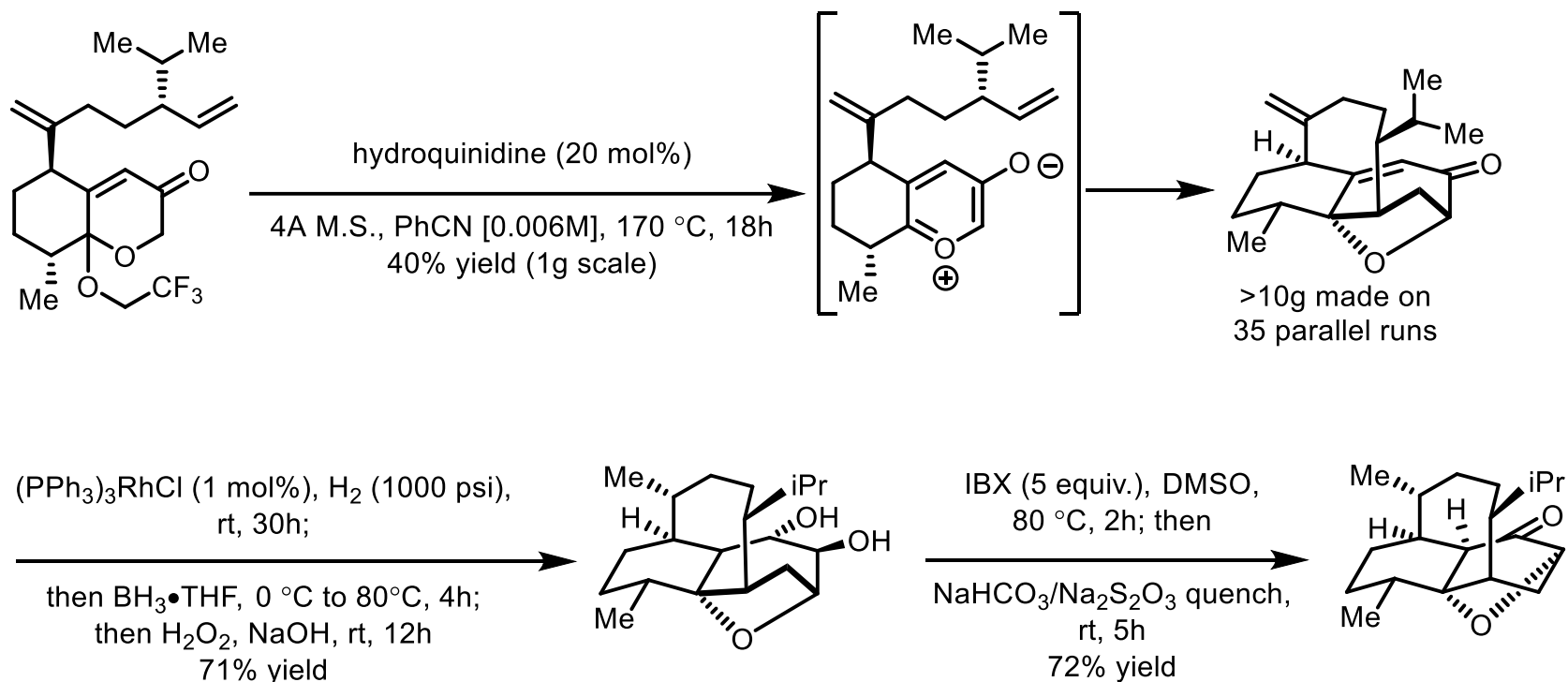


*various amine bases tried, as well as
acids, just heat, various solvents, MW
heating, etc.*

Li's Synthesis of (–)-Vinigrol (2019)

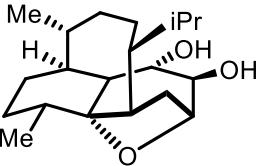
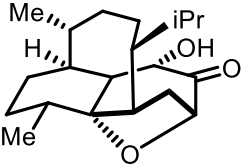
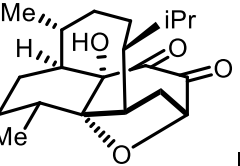
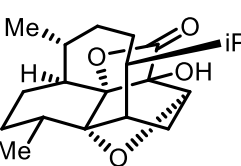
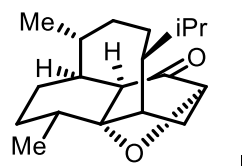
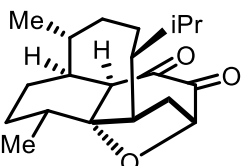


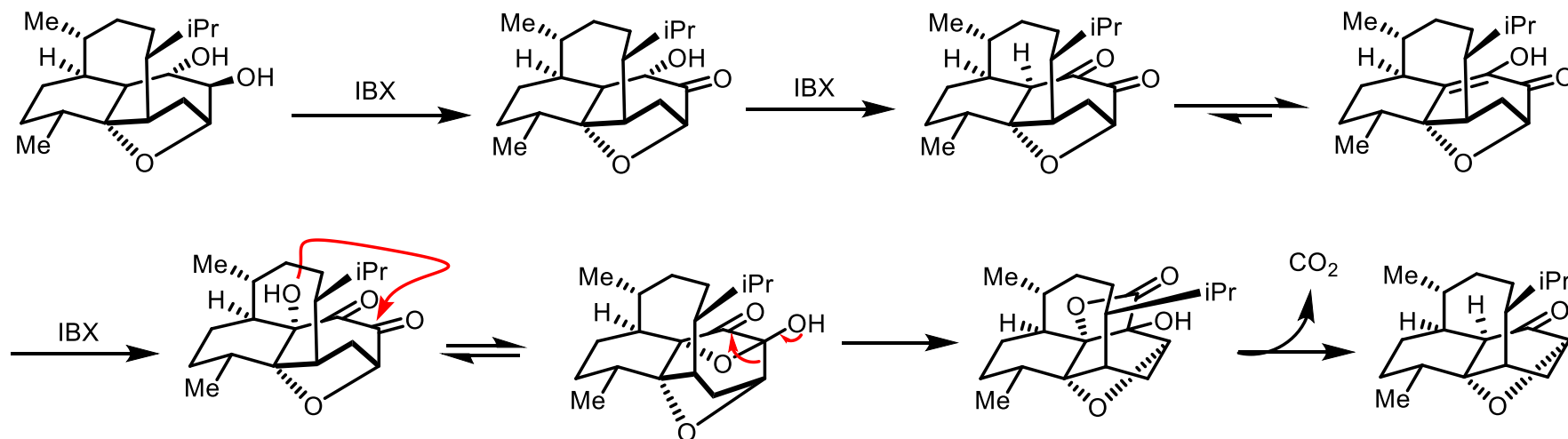
Li's Synthesis of (–)-Vinigrol (2019)



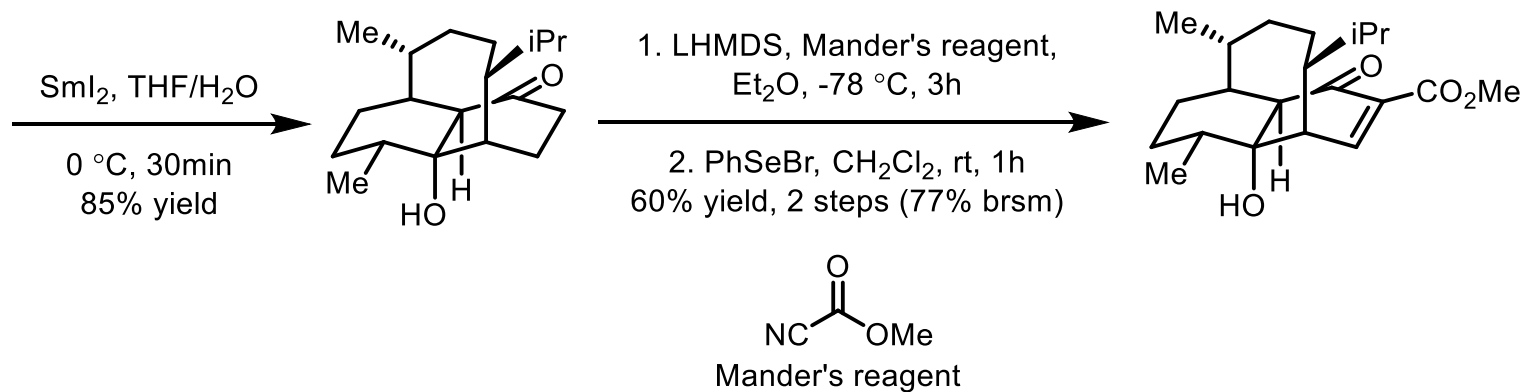
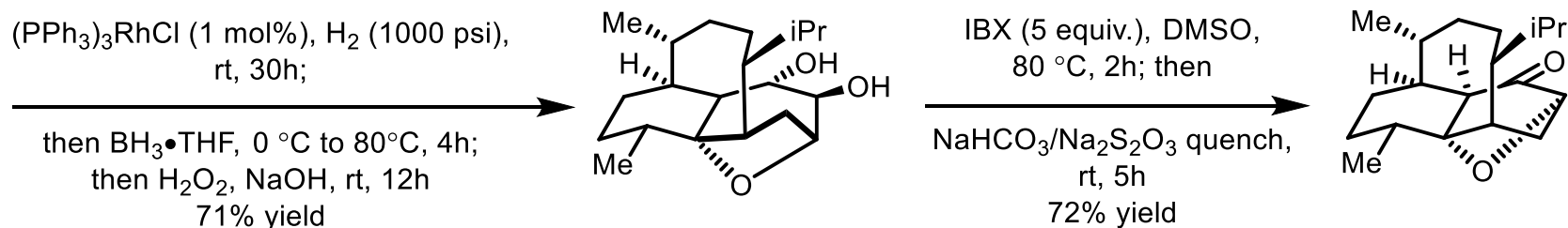
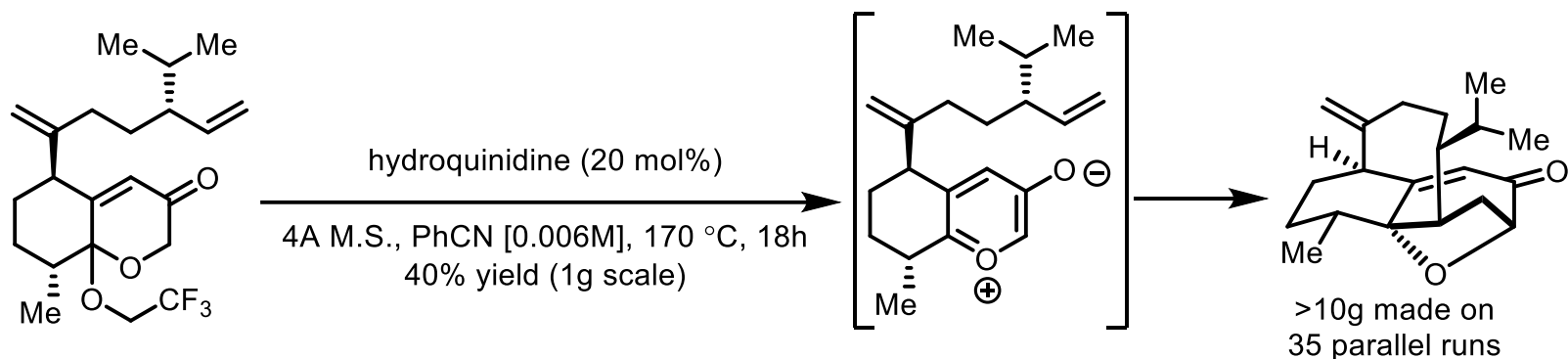
Li's Synthesis of (–)-Vinigrol (2019)

expected pdt

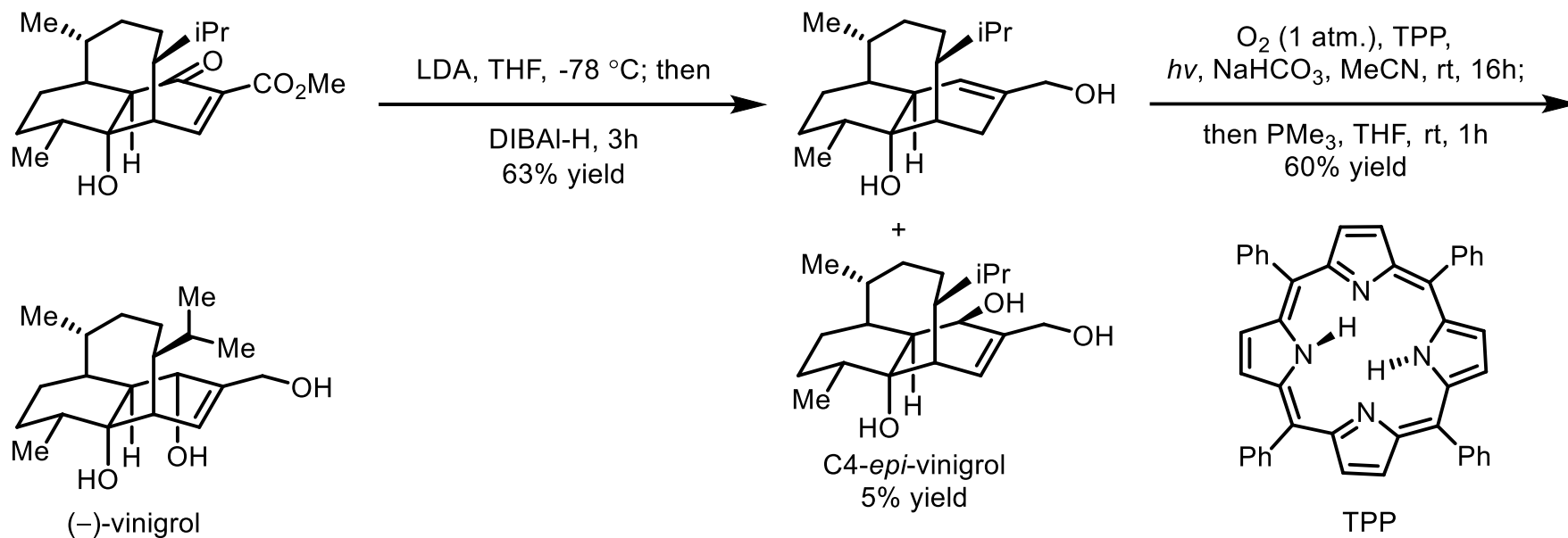
	[ox]					
IBX (2 equiv.), DMSO, 80 °C, 2h		30%	30%		10%	
DMP, Parikh-Doering, Jones, PCC, Ley, Moffat, Corey-Kim, Swern		exclusive product				
IBX (5 equiv.), DMSO, 80 °C, 2h				12%	72%	



Li's Synthesis of (–)-Vinigrol (2019)

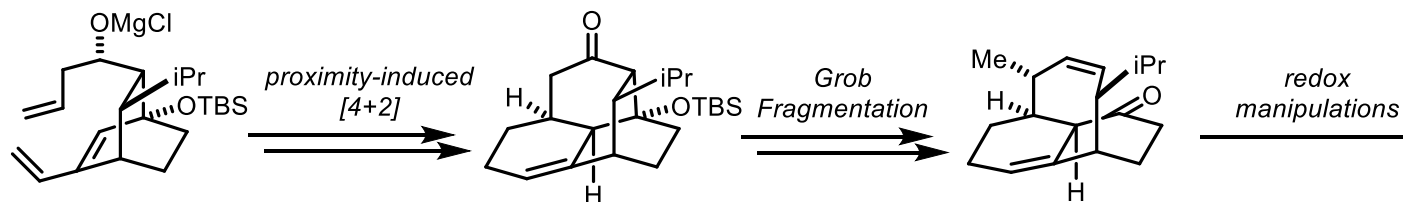


Li's Synthesis of (–)-Vinigrol (2019)

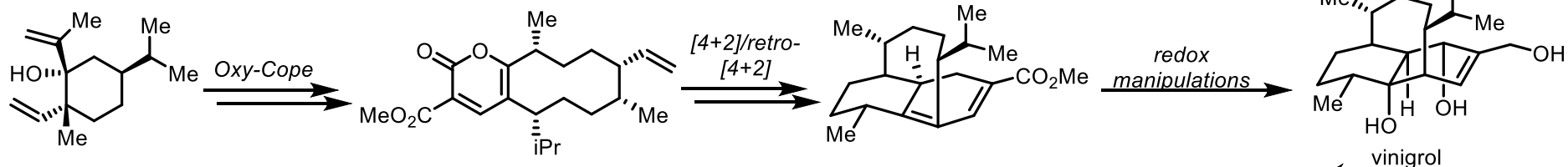


Summary

Phil Baran, 2008



Tuoping Luo, 2019



Chuang-Chuang Li, 2019

