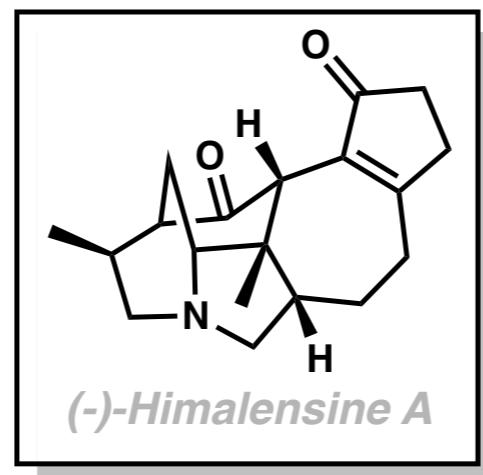
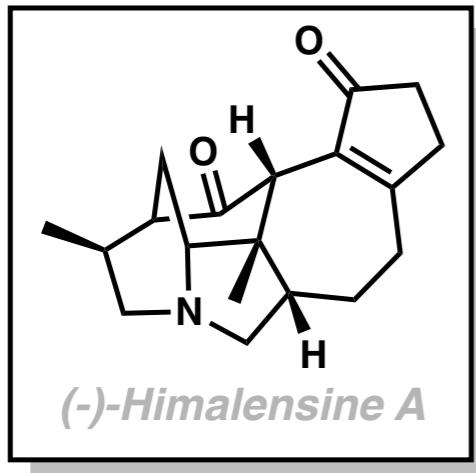


# *Dixon's Synthesis of (-)-Himalensine A*



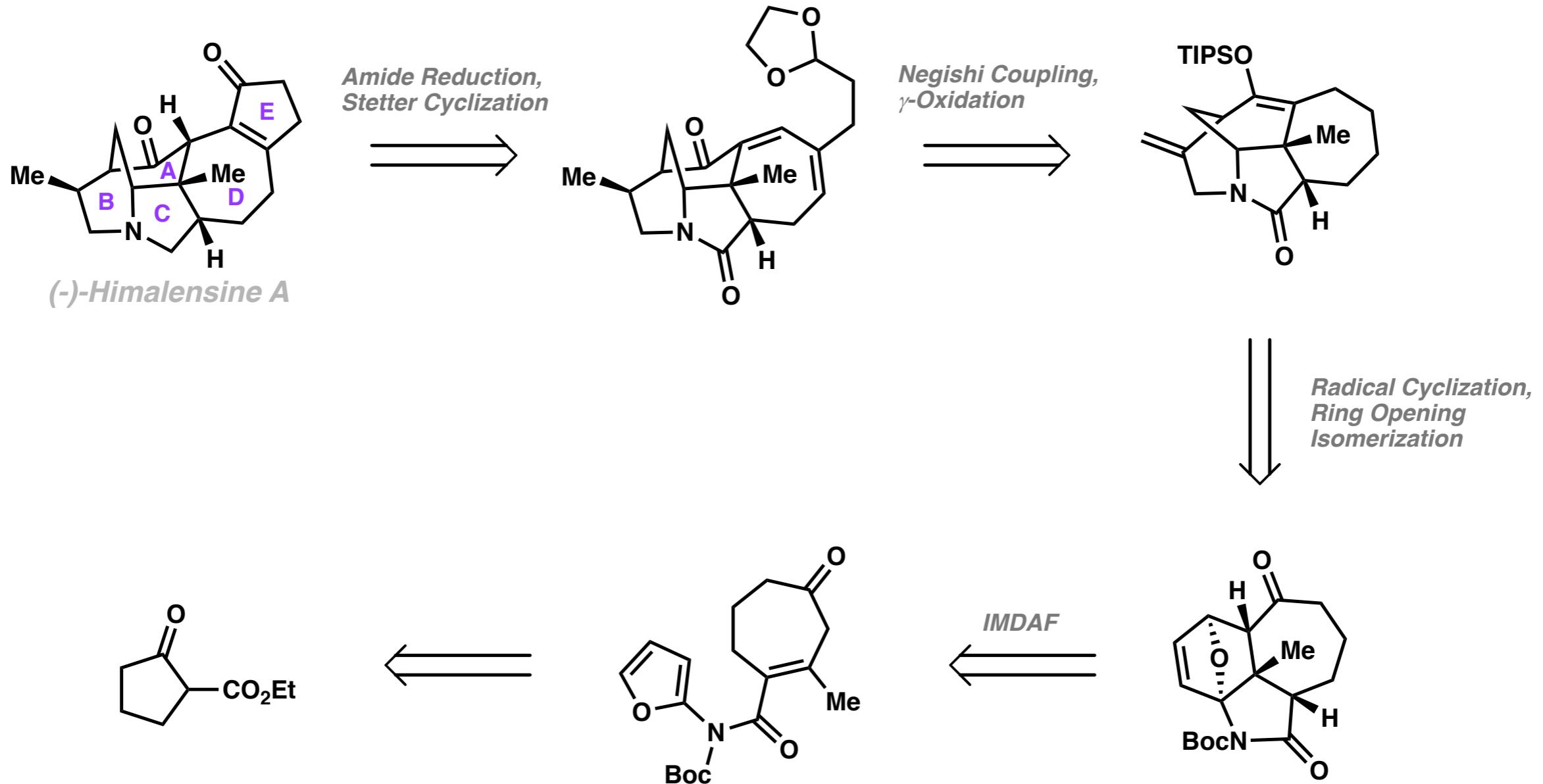
*Johanna Masterson  
Sorensen Group Meeting  
November 13, 2020*

# (-)-Himalensine A

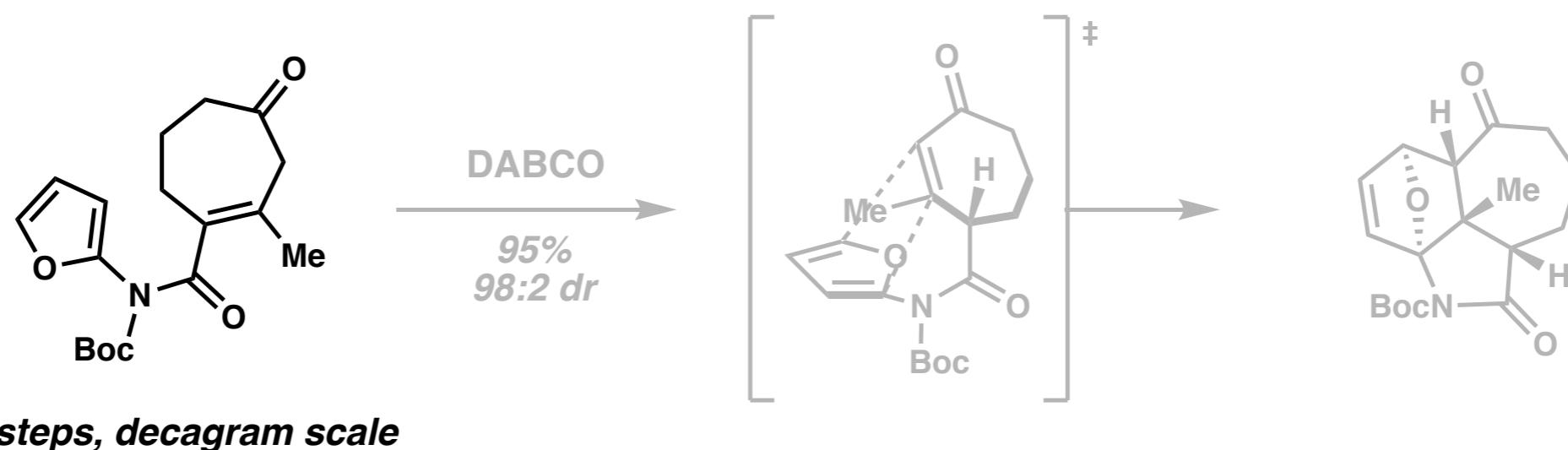


- Daphniphyllum alkaloid belonging to the Calyciphylline A-type subfamily
- First isolated in 2016
- First synthesis: Dixon (2017, 22 steps)
- Two additional syntheses: Xu (2019, 14 steps), (Gao, 2019, racemic)

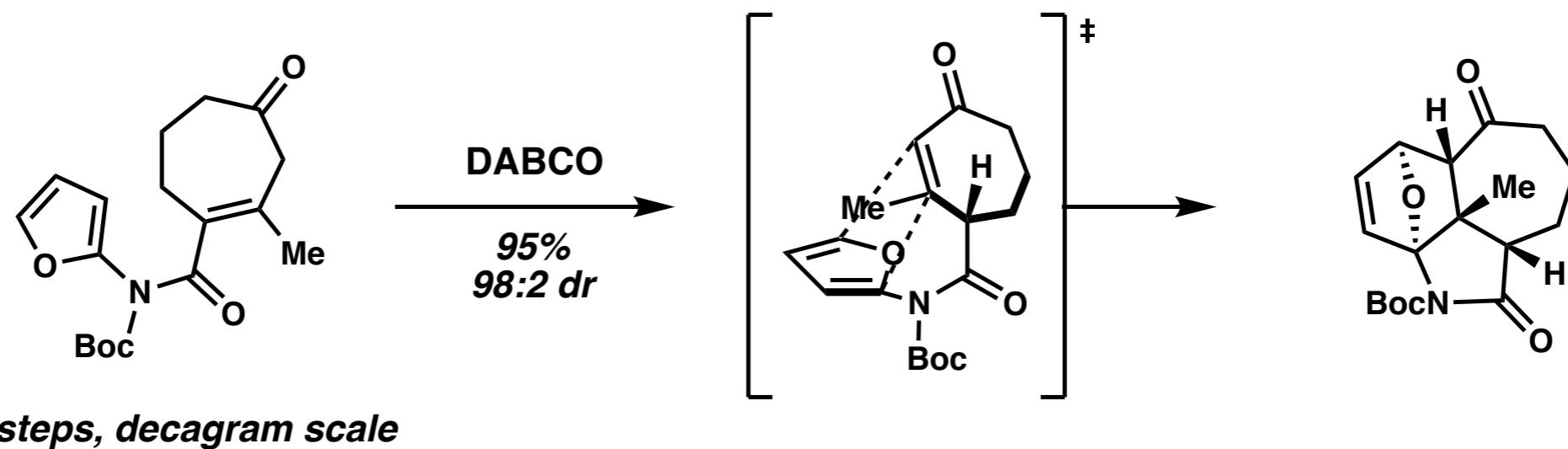
# Retrosynthetic Strategy



# *Development of Enantioselective IMDAF*

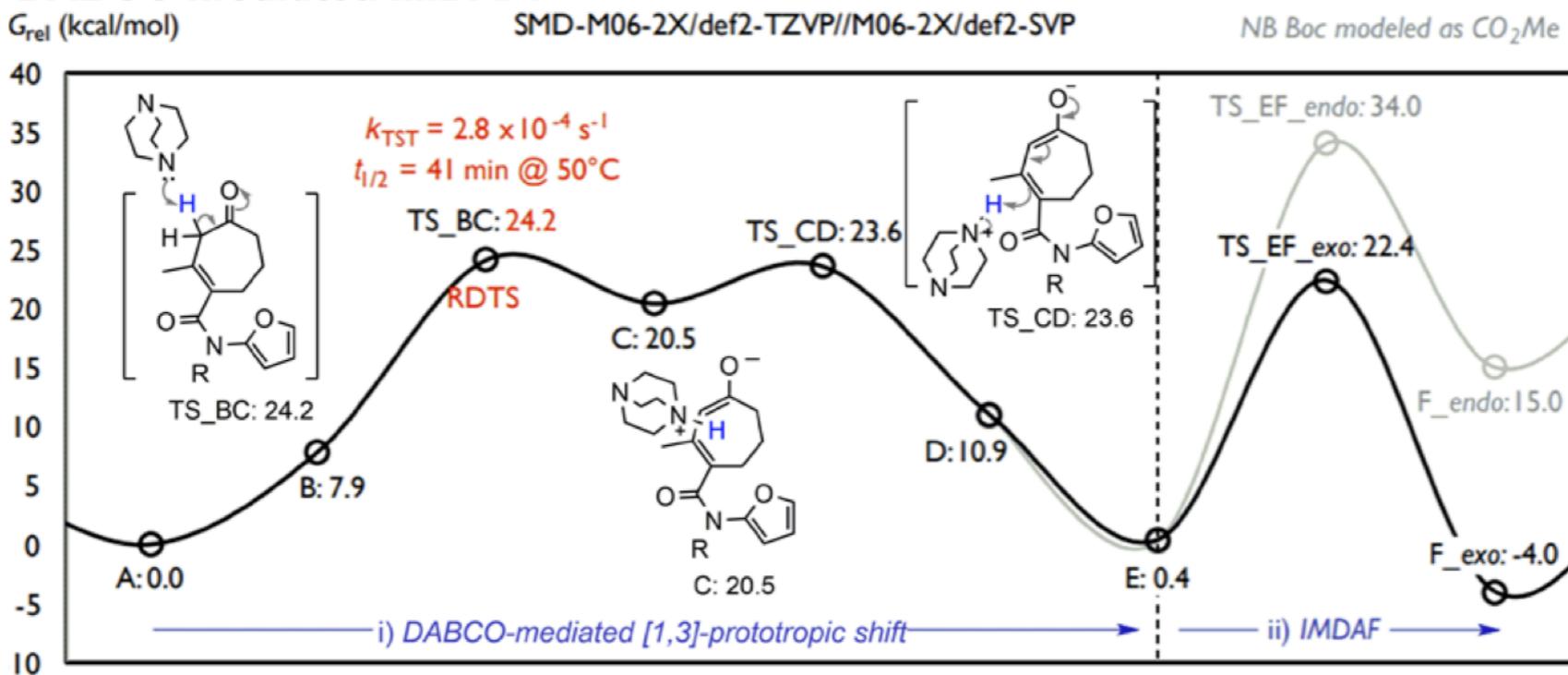


# *Development of Enantioselective IMDAF*

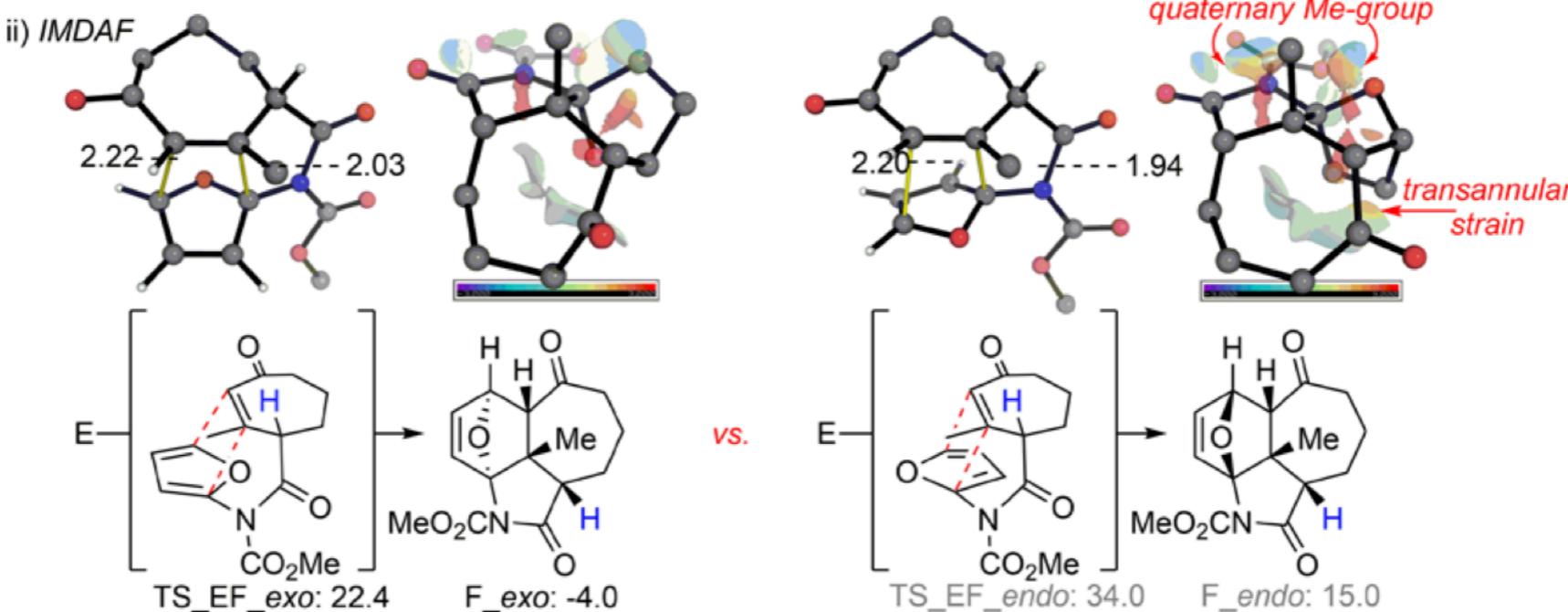


# Development of Enantioselective IMDAF

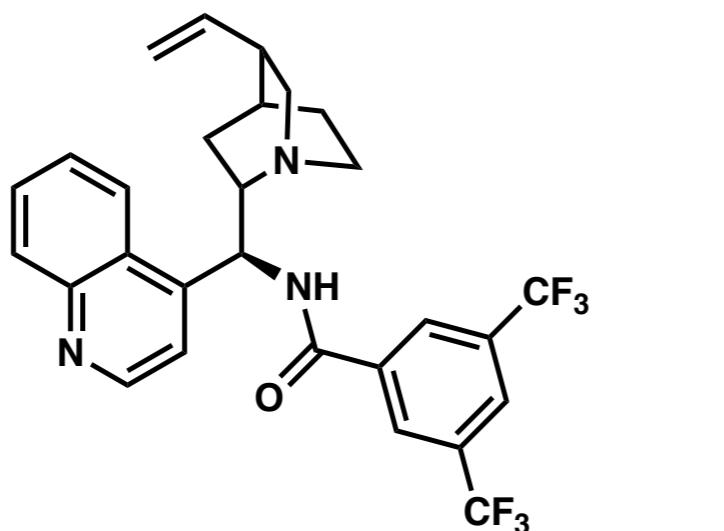
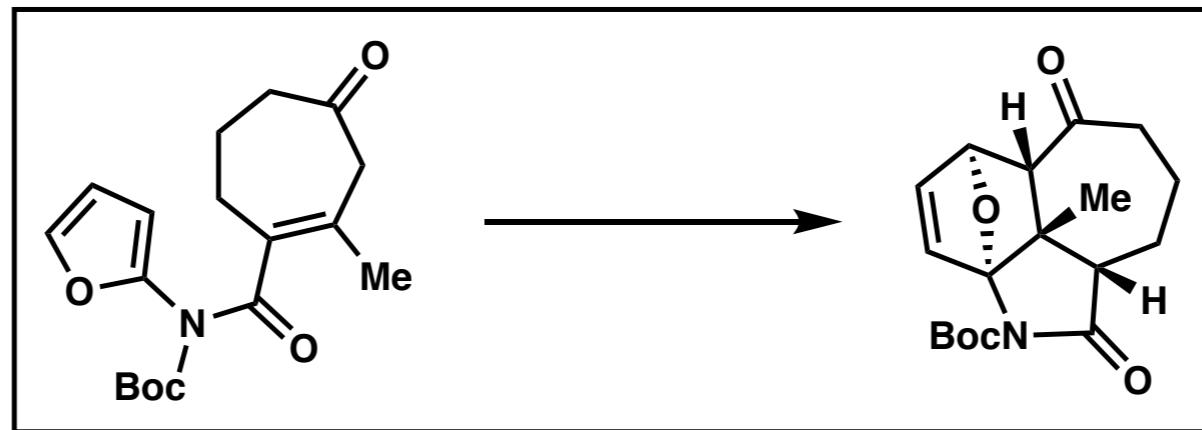
## DABCO mediated IMDAF:



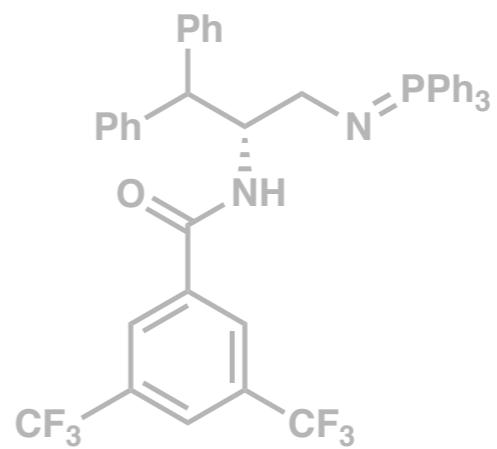
## Diels-Alder endo/exo selectivity:



# *Development of Enantioselective IMDAF*

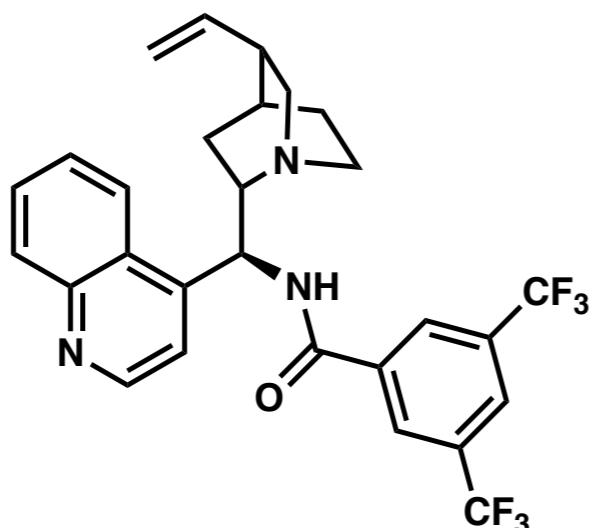
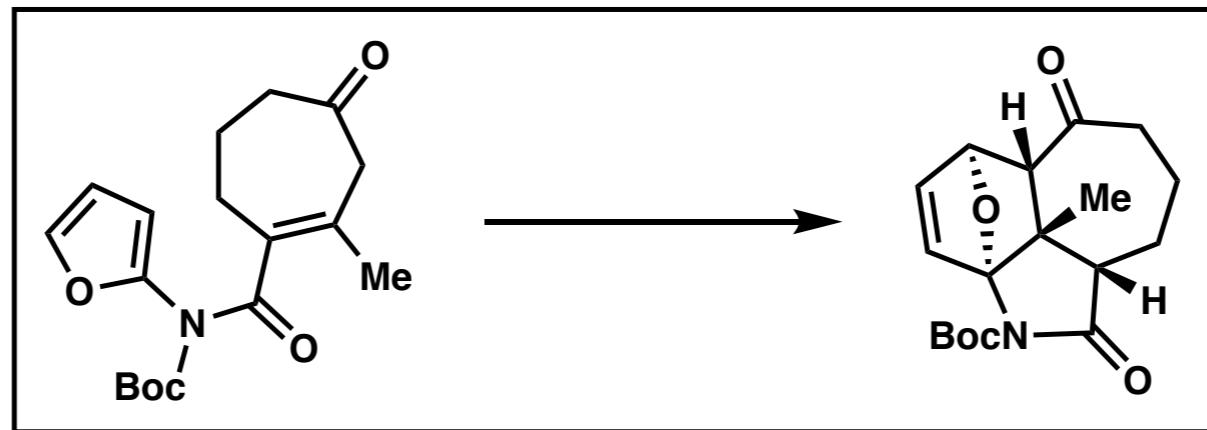


**7 days  
20 mol%  
73% ee**

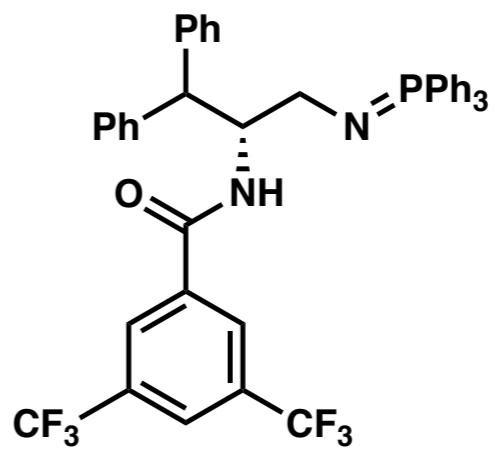


*24 hours  
5 mol%  
99% ee, 86% yield  
4 gram scale*

# *Development of Enantioselective IMDAF*

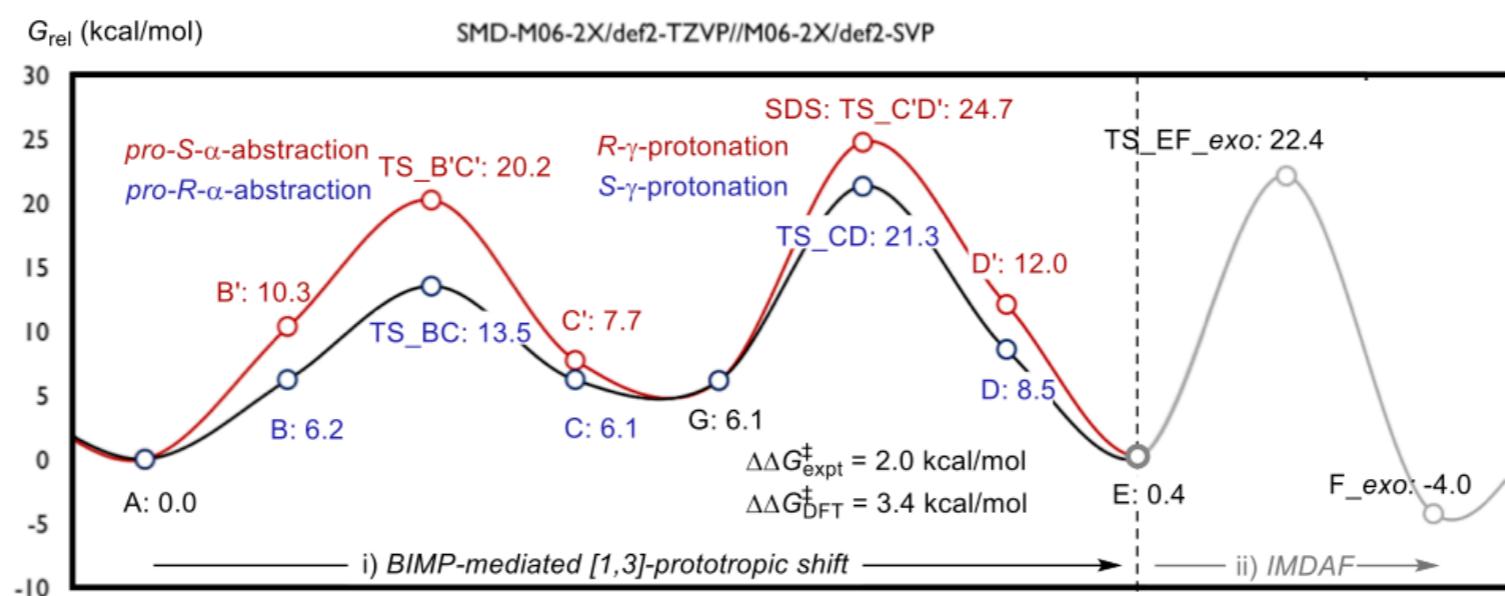
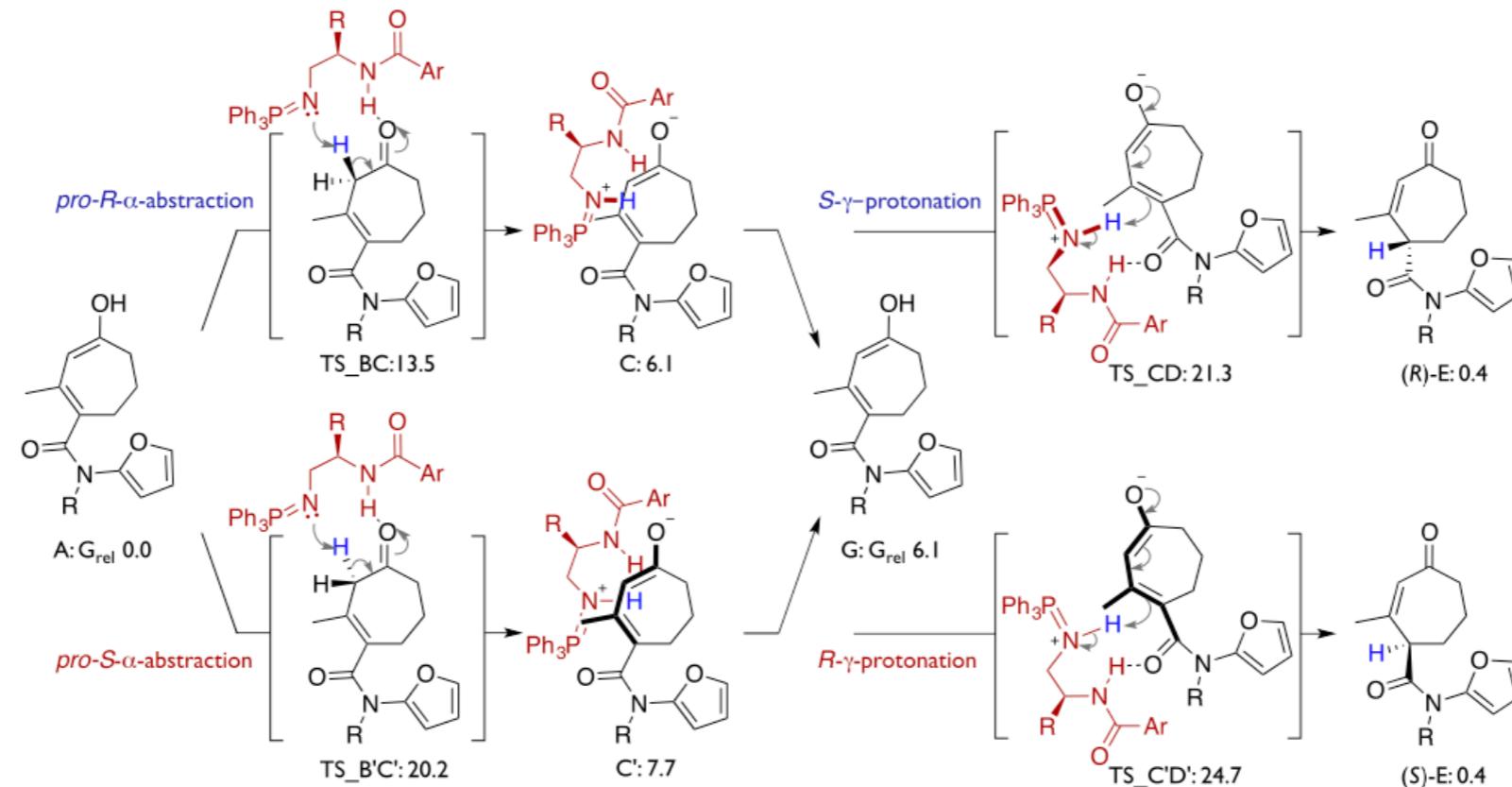


**7 days  
20 mol%  
73% ee**

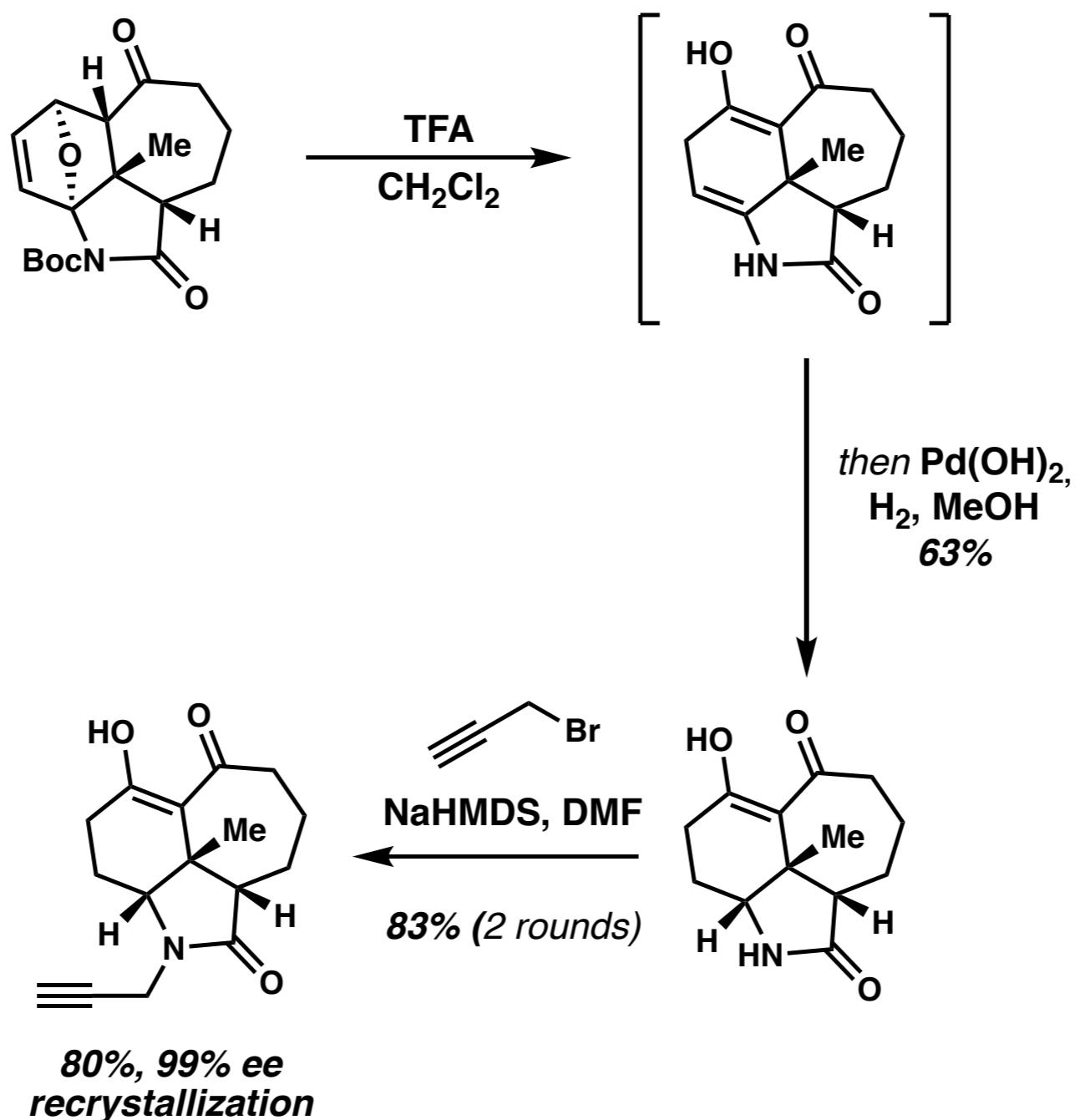


**24 hours  
5 mol%  
99% ee, 86% yield  
4 gram scale**

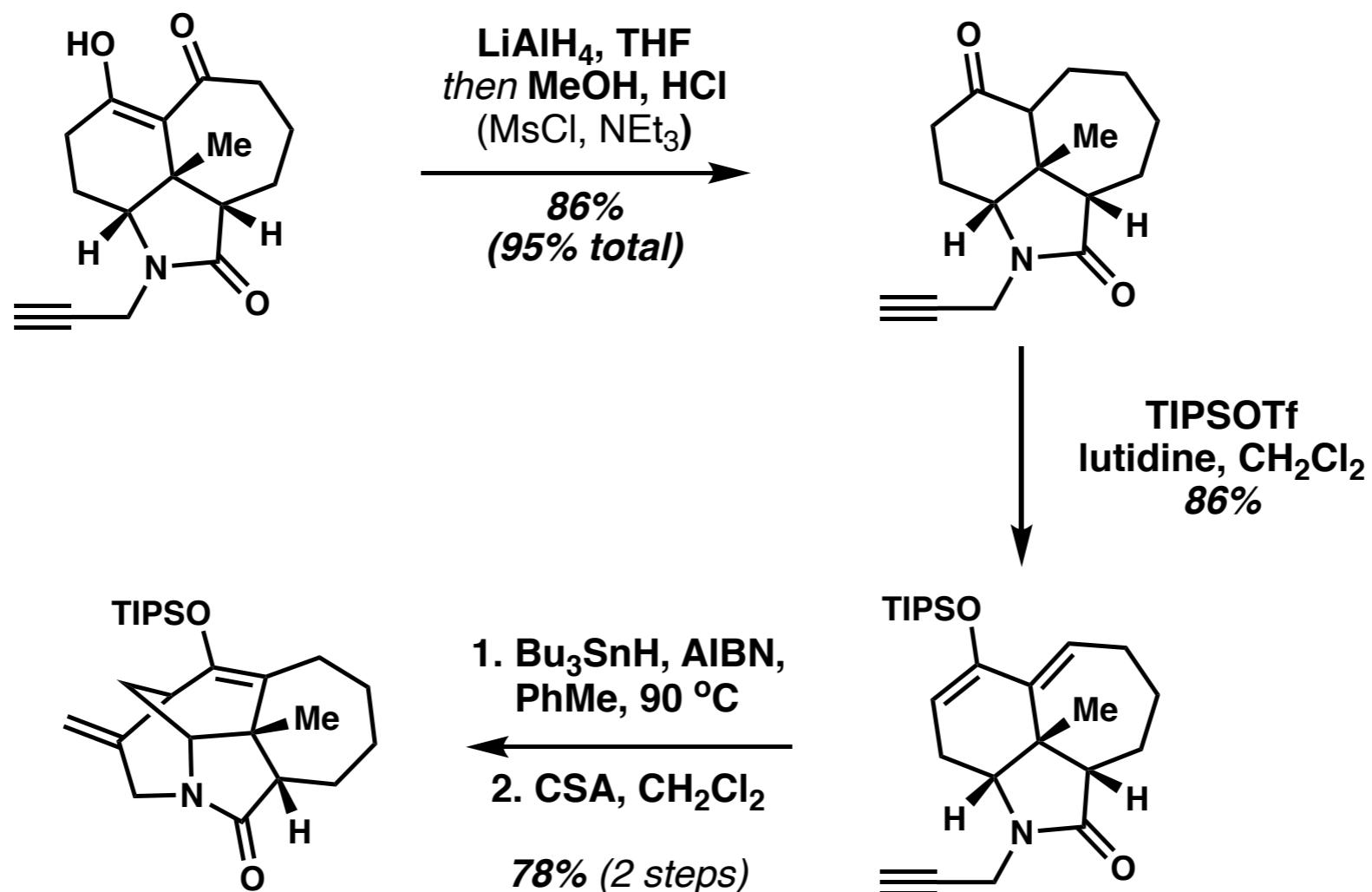
# Development of Enantioselective IMDAF



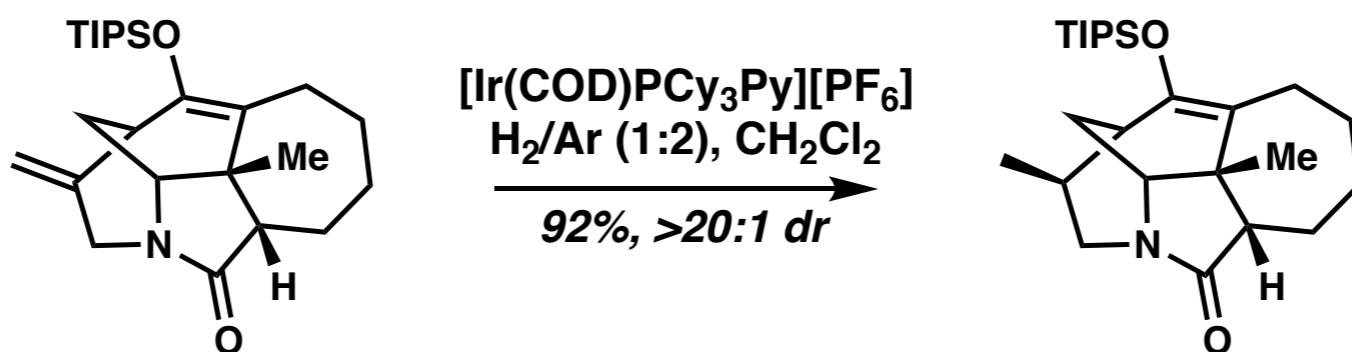
## Elaboration to (-)-Himalensine A



## *Elaboration to (-)-Himalensine A*

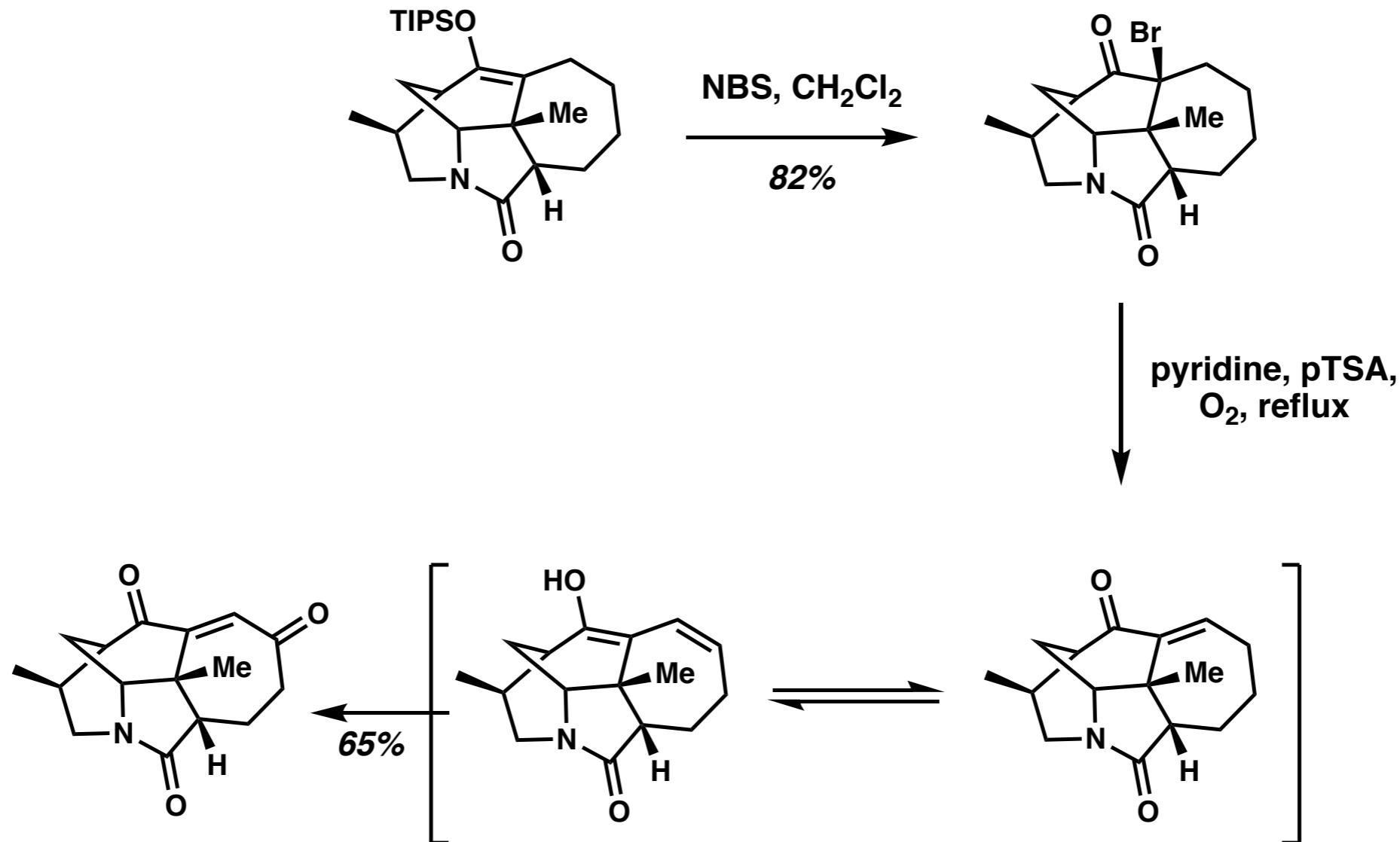


## *Elaboration to (-)-Himalensine A*

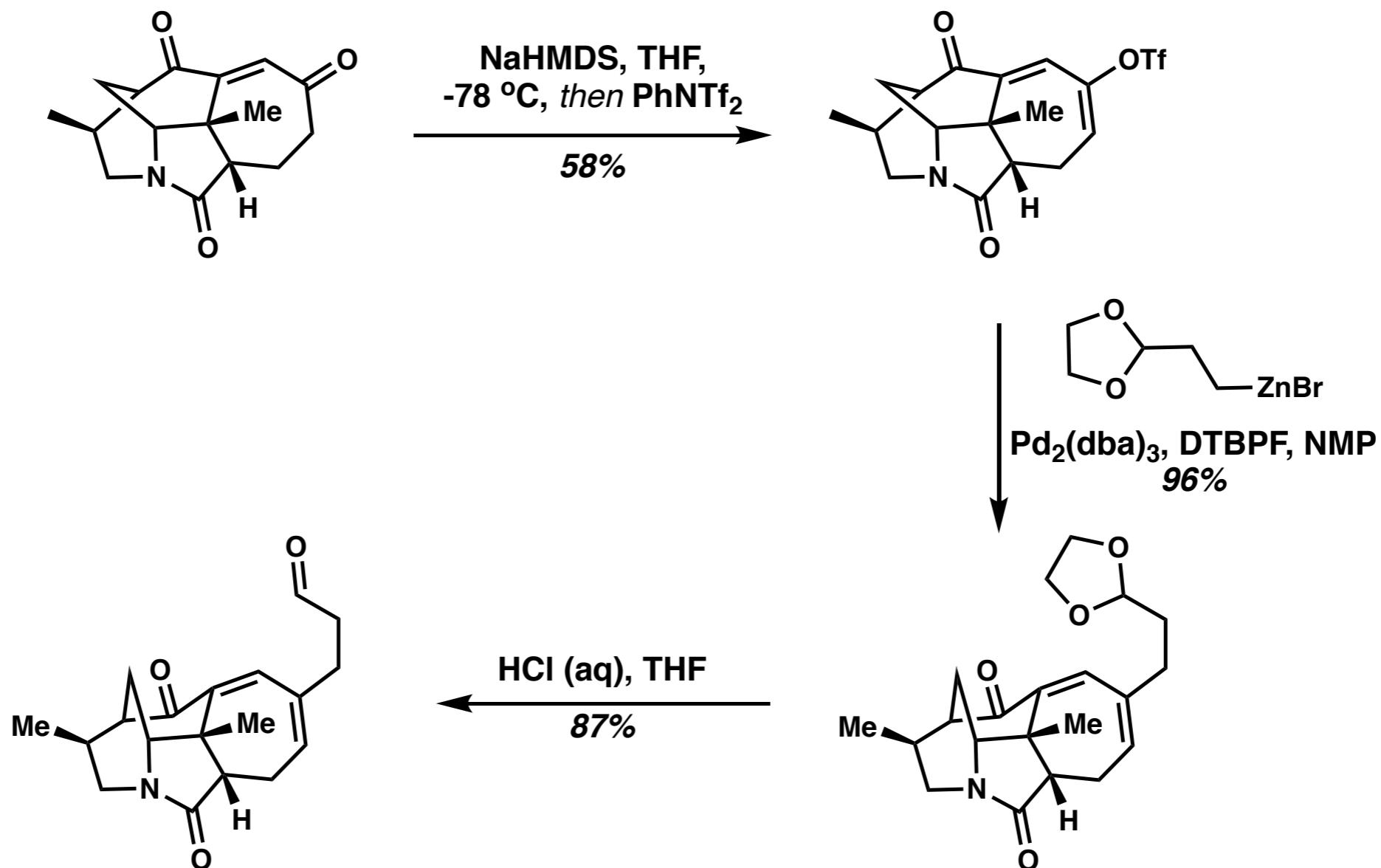


<i>via:</i> Me OTIPS	pressure / mbar	dr
	1086 <sup>a)</sup>	2.2:1
	1055 <sup>b)</sup>	2.8:1
	1029 <sup>c)</sup>	3.4:1
	1029 <sup>c)</sup> (50% Ar)	6.8:1
	<b>1029<sup>c)</sup> (66% Ar)</b>	<b>&gt;20:1</b>

## *Elaboration to (-)-Himalensine A*



## *Elaboration to (-)-Himalensine A*



## *Elaboration to (-)-Himalensine A*

