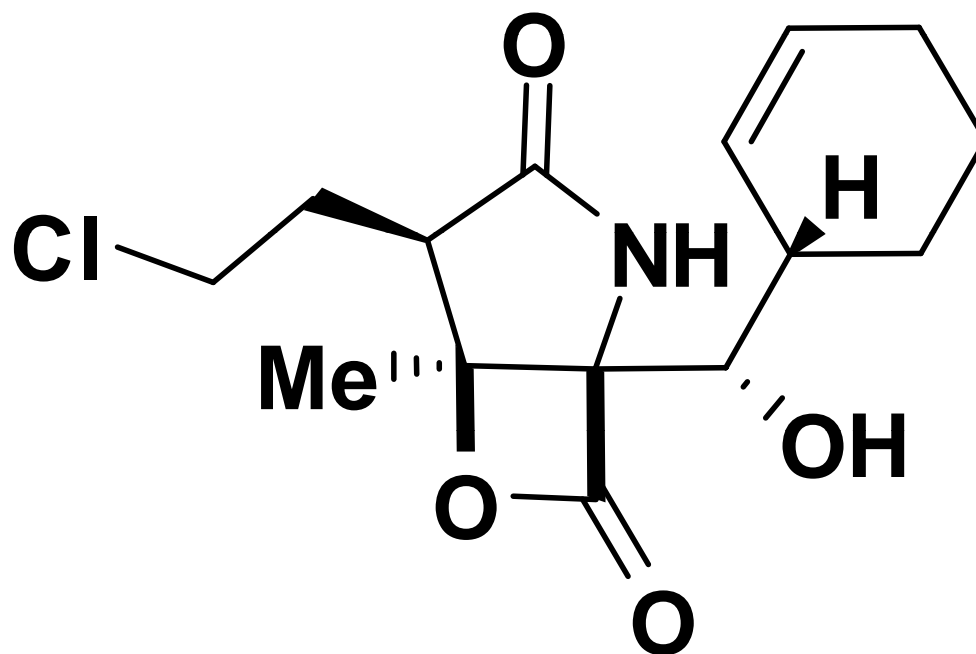


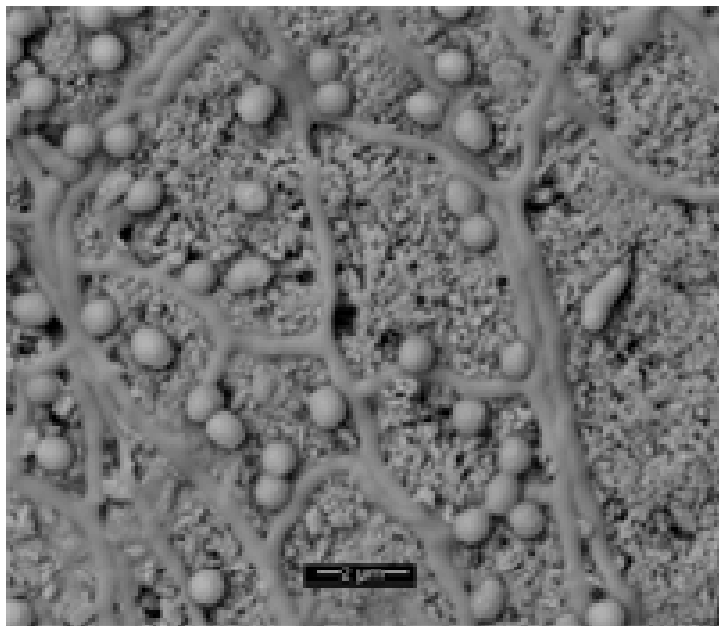
# Salinosporamide A

Anne-Marie Dechert

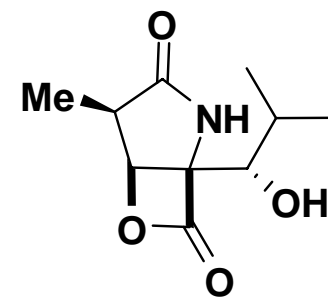
August 1, 2007



# Salinosporamide A

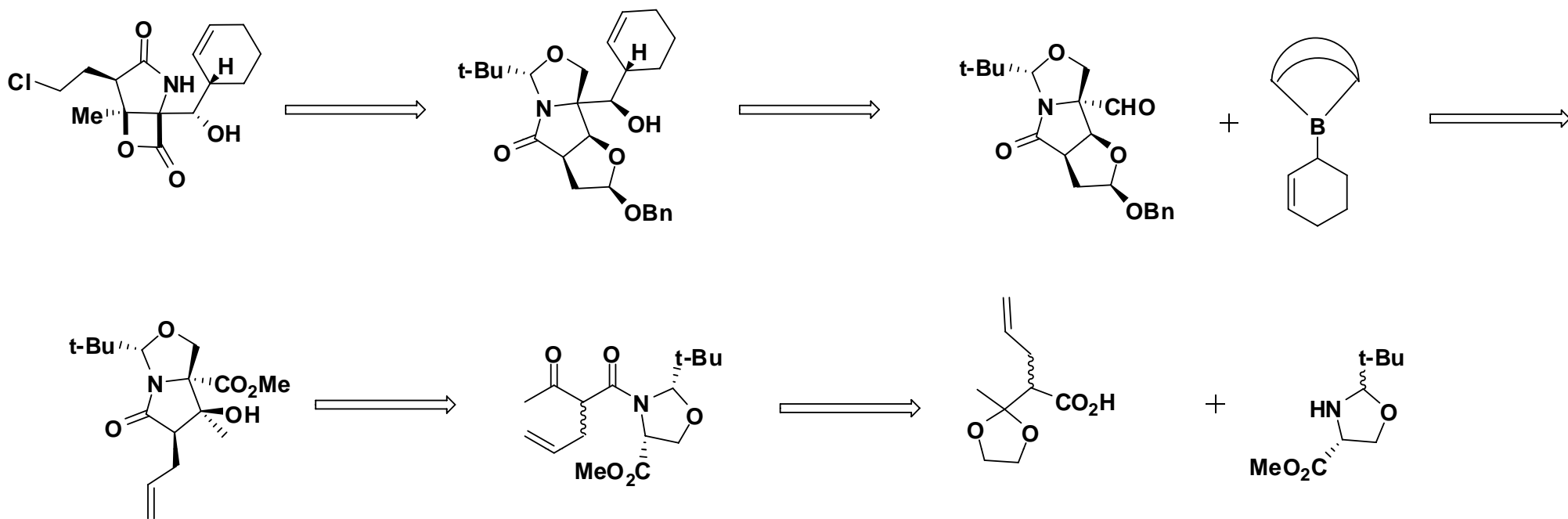


- Derived as a secondary metabolite from the marine actinomycete *Salinispora tropica*
- Displays high in vitro cytotoxicity against the 20S proteasome
- Approximately 35 times more potent than *omuralide*
- Currently in clinical trials for the treatment of cancer

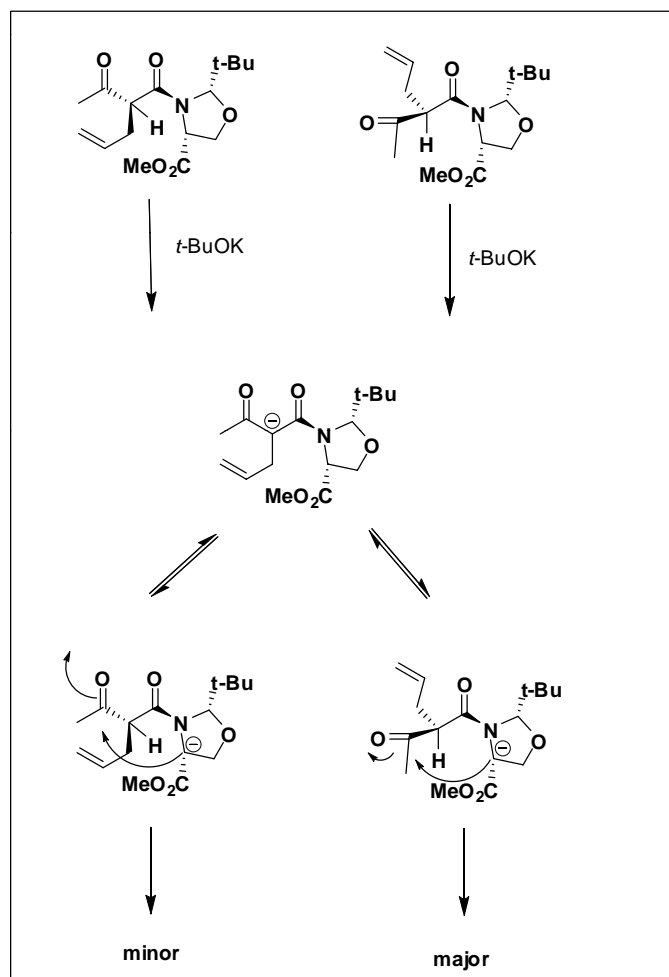
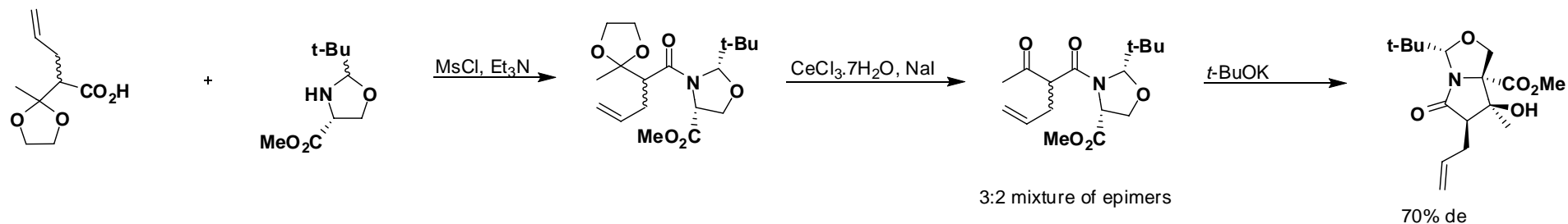


omuralide

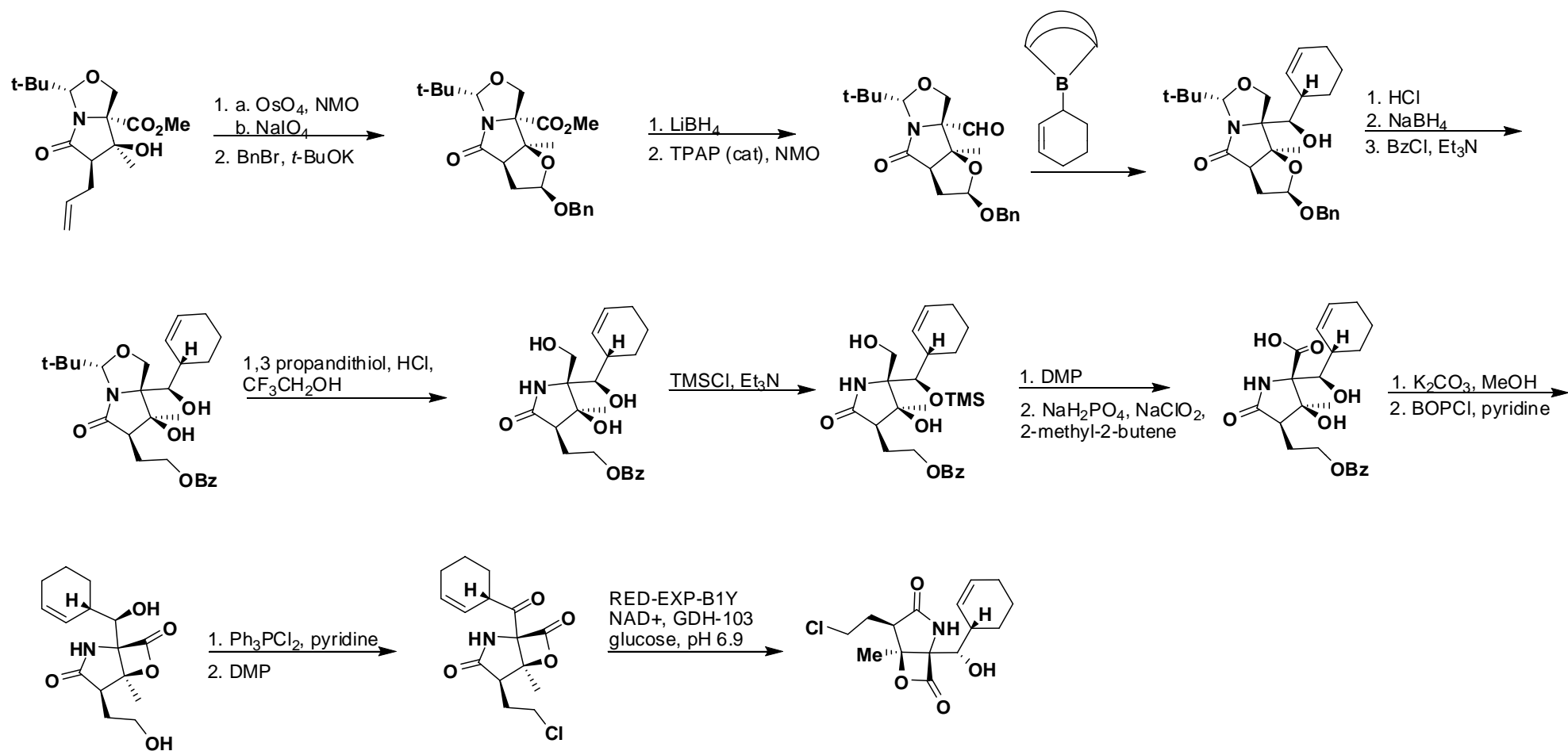
# Macheria's Retrosynthesis



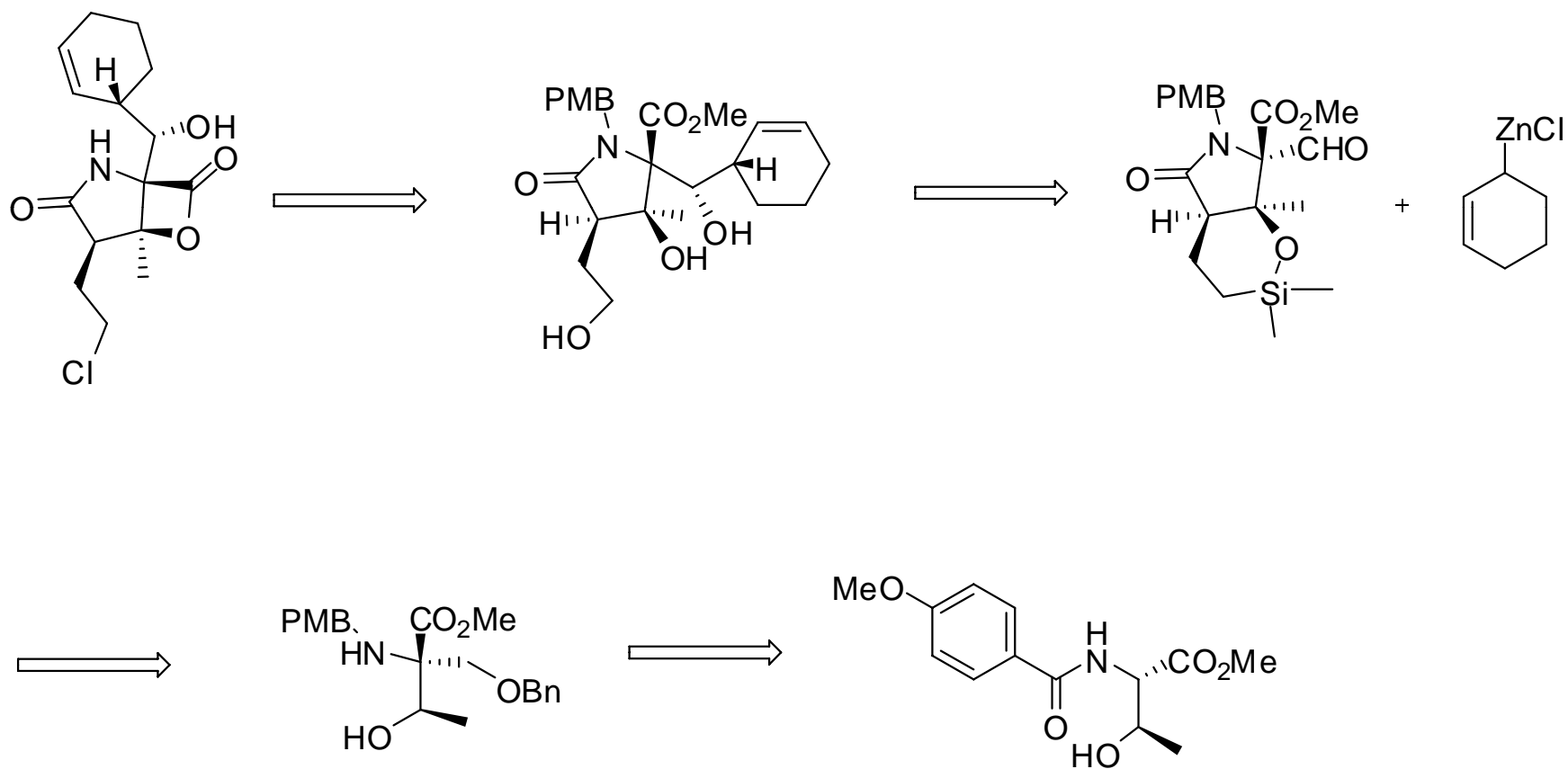
# Macheria's Synthesis



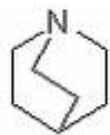
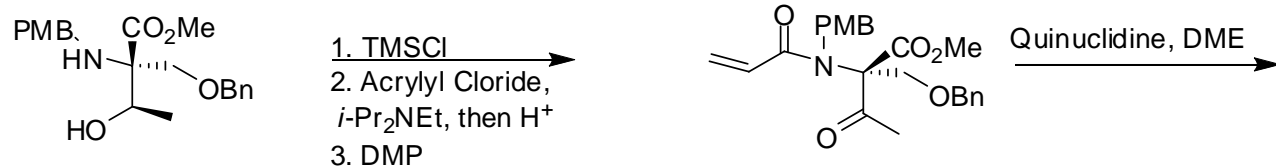
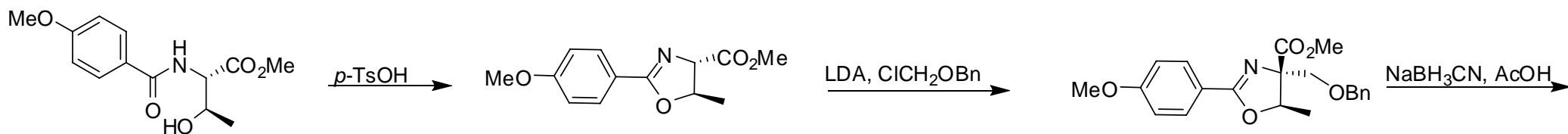
# Macheria's Synthesis



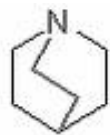
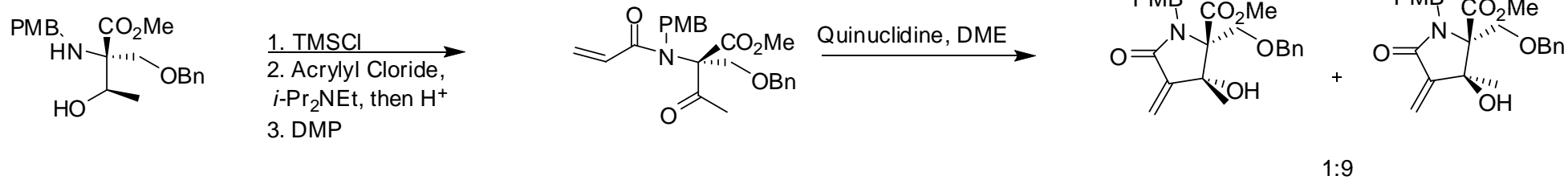
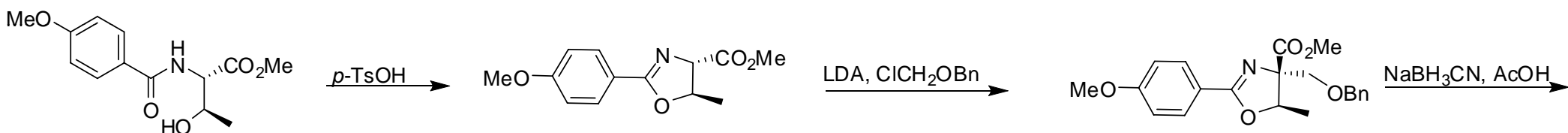
# Corey's Retrosynthesis



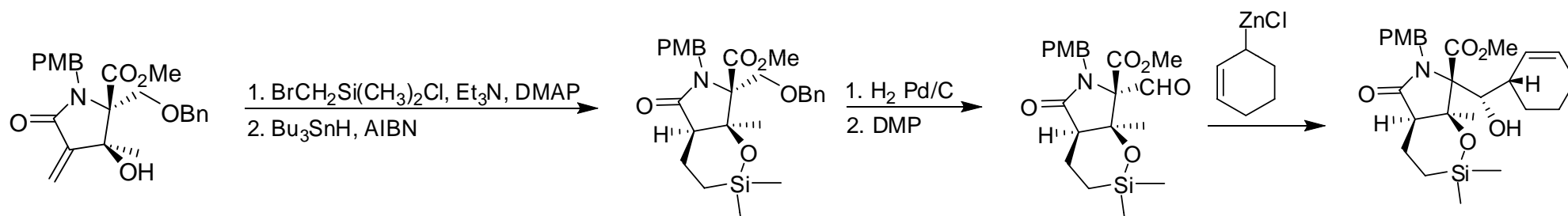
# Corey's First Synthesis



# Corey's First Synthesis



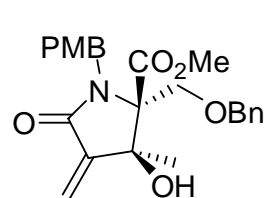
# Corey's First Synthesis



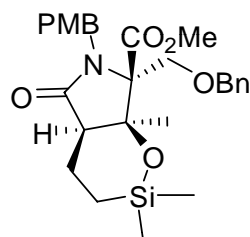
KF, KHCO<sub>3</sub>, H<sub>2</sub>O<sub>2</sub>  
THF-MeOH



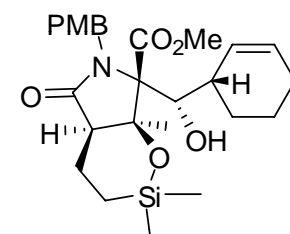
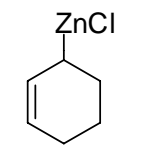
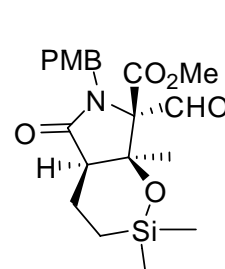
# Synthesis



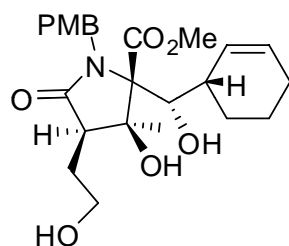
1.  $\text{BrCH}_2\text{Si}(\text{CH}_3)_2\text{Cl}$ ,  $\text{Et}_3\text{N}$ , DMAP  
2.  $\text{Bu}_3\text{SnH}$ , AIBN



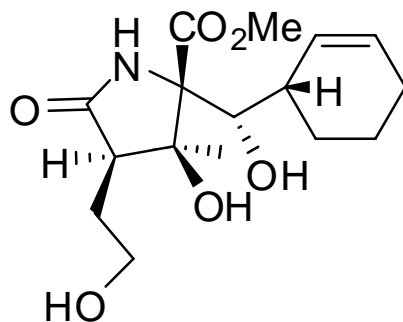
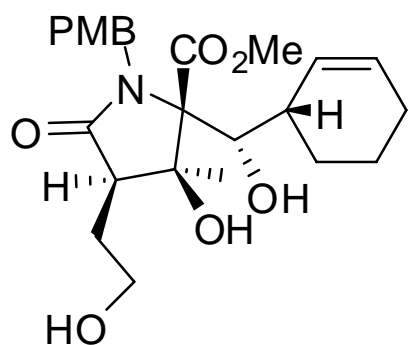
1.  $\text{H}_2$  Pd/C  
2. DMP



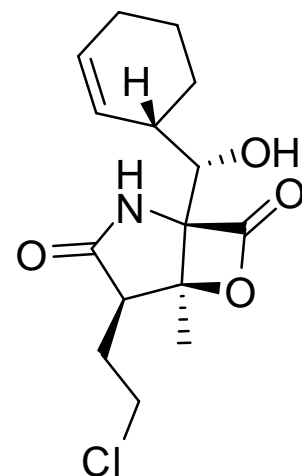
$\text{KF}$ ,  $\text{KHCO}_3$ ,  $\text{H}_2\text{O}_2$   
THF-MeOH



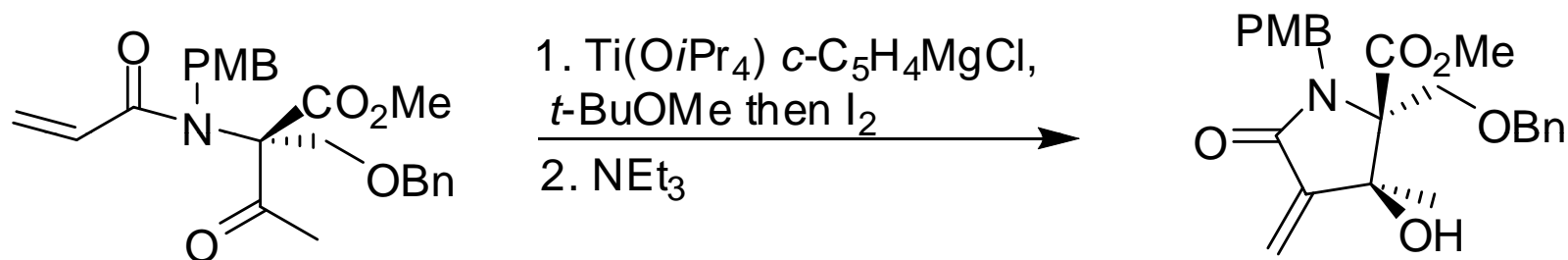
# End Game



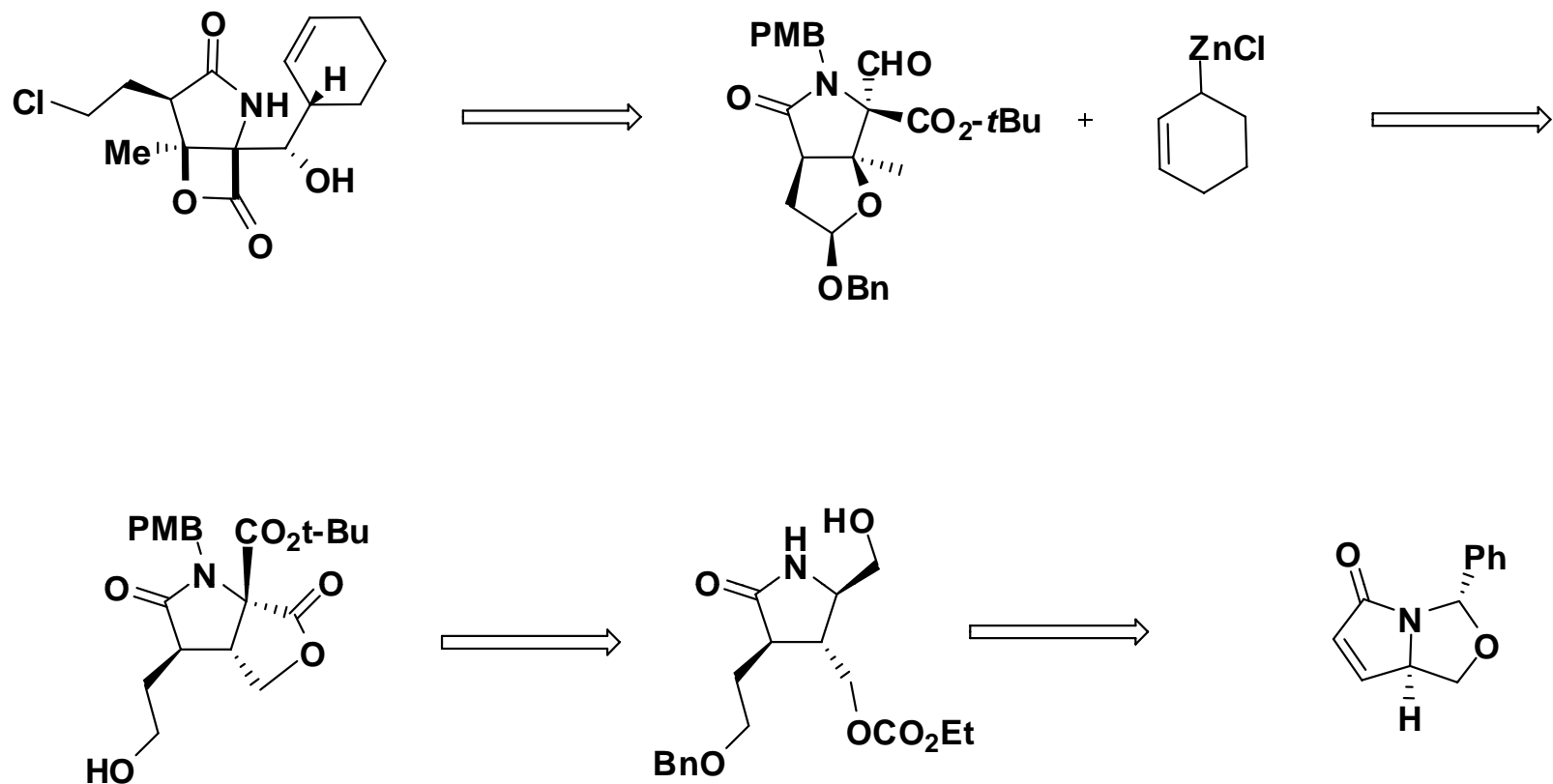
1. 3 N LiOH  
2. BOPCl, pyridine  
3. Ph<sub>3</sub>PCl<sub>2</sub>, pyridine
- 



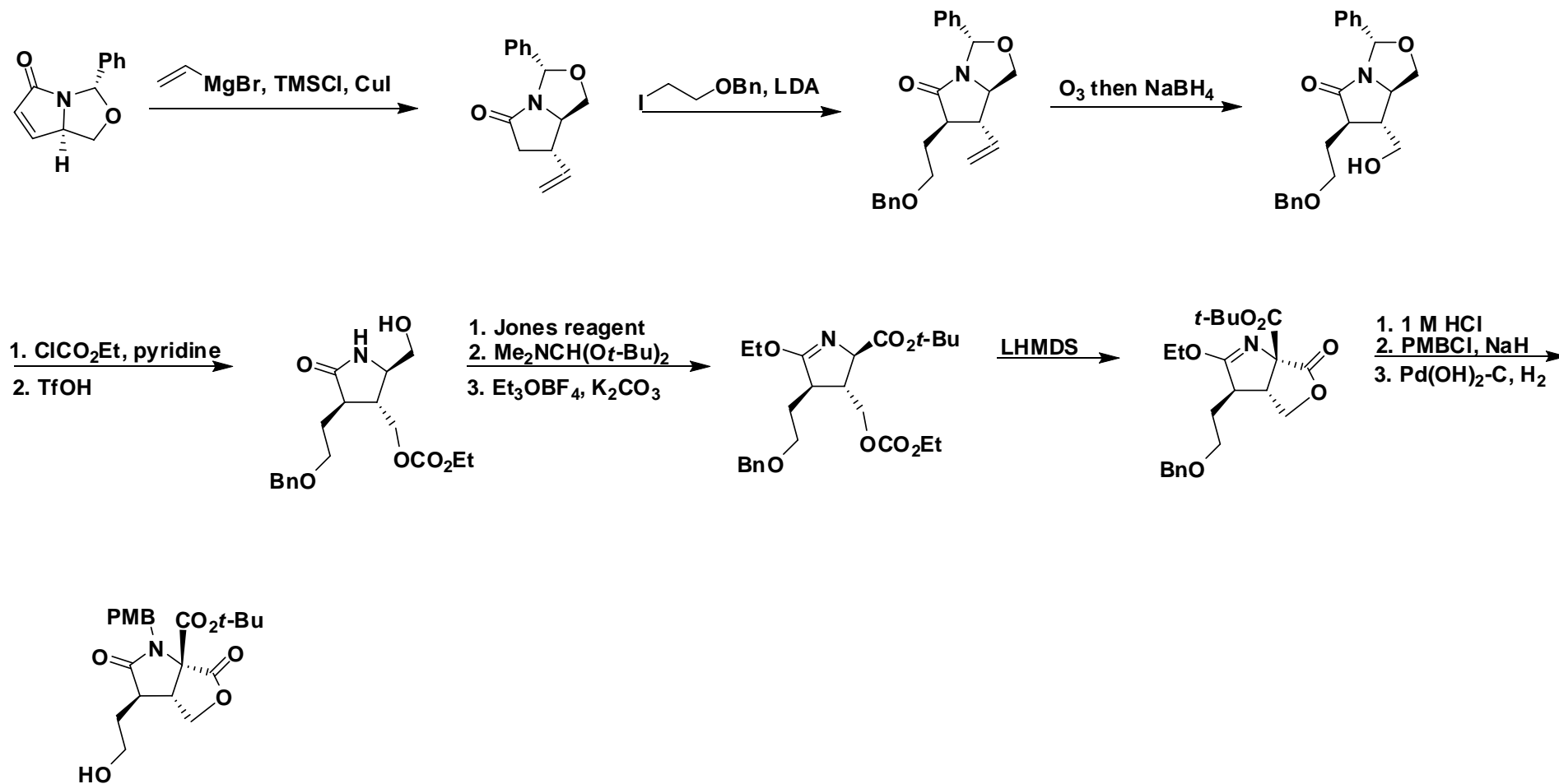
# Synthesis of analogues by Corey: The Key Step



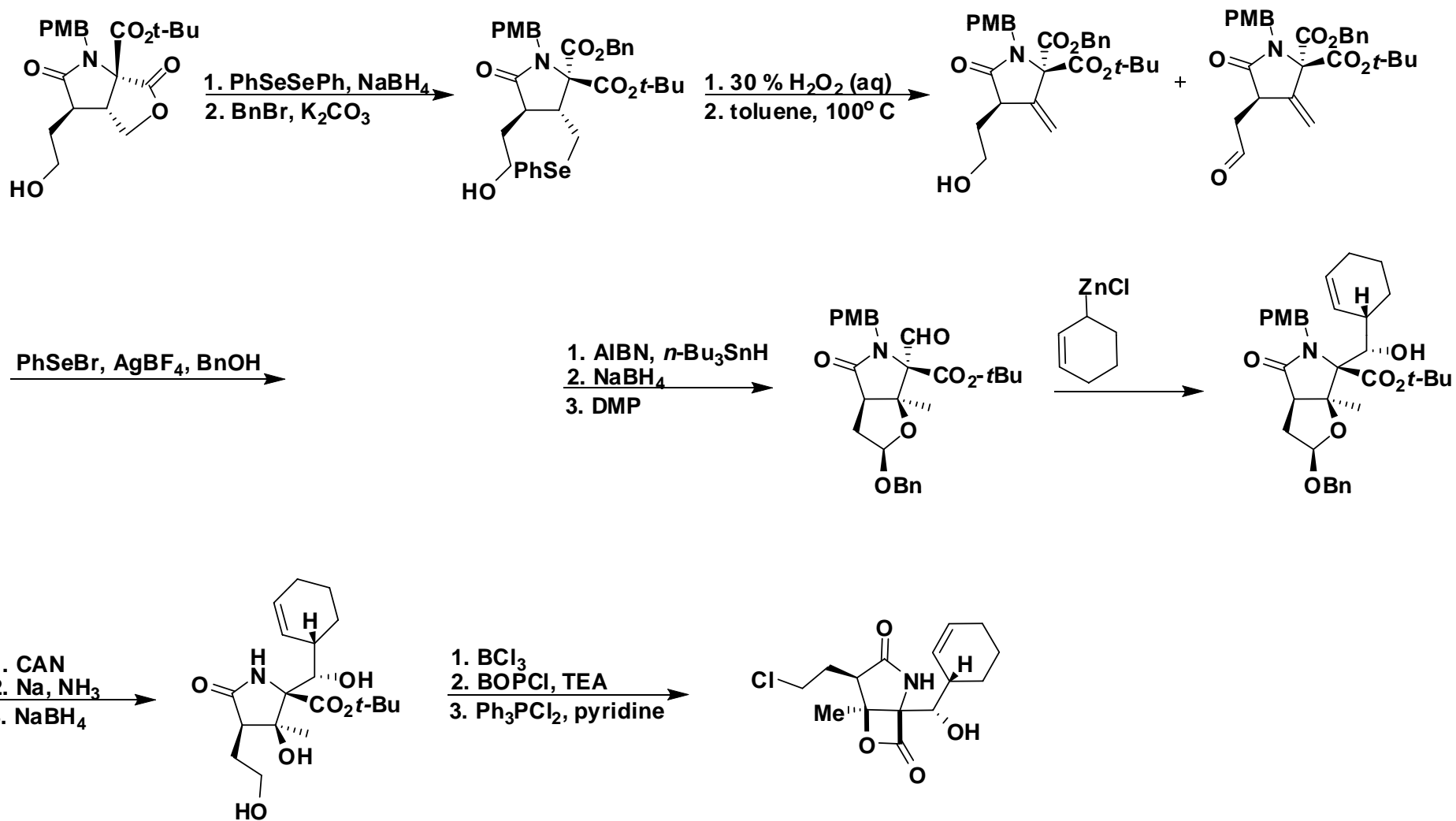
# Danishefsky's Retrosynthesis



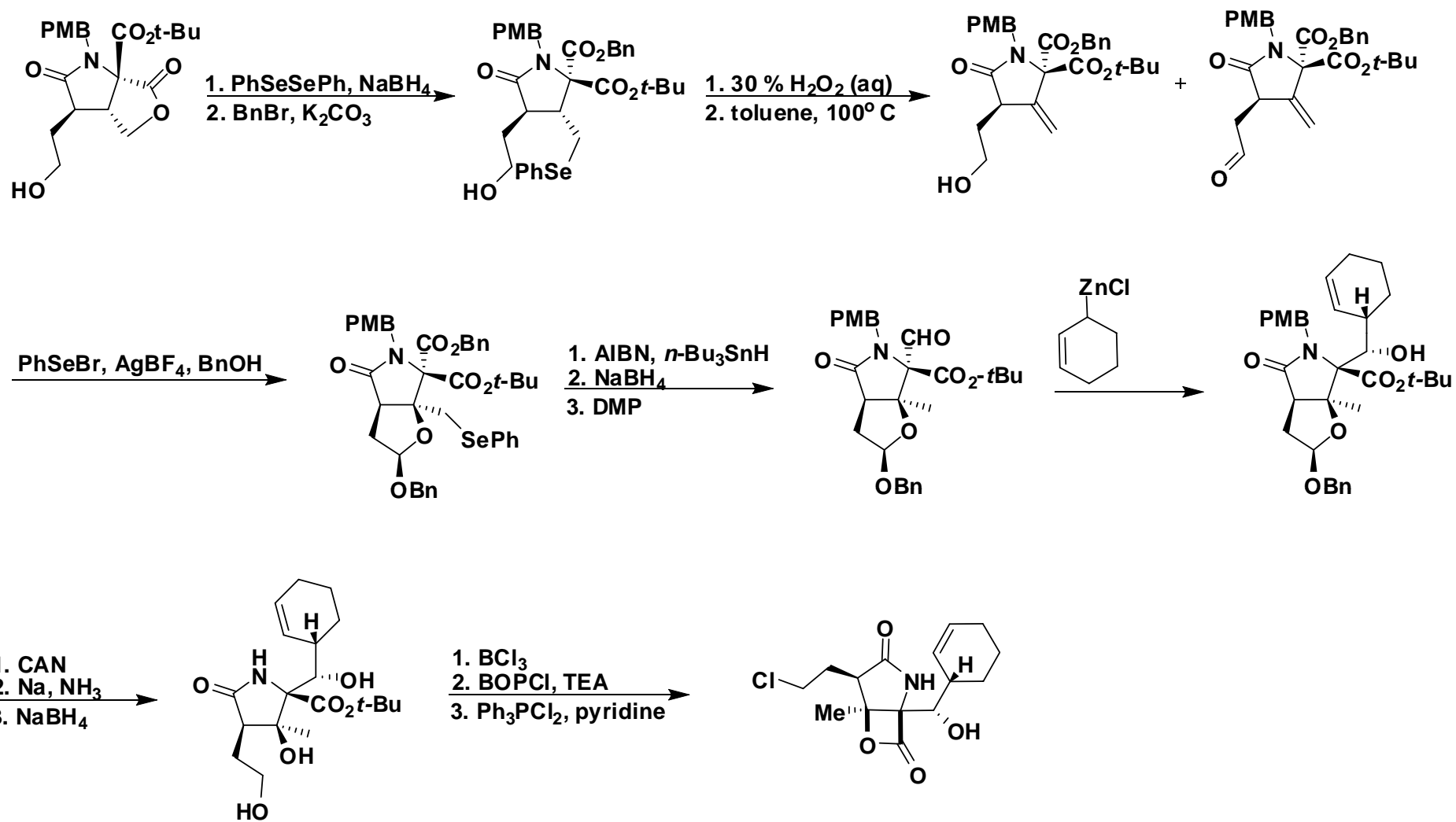
# Danishefsky's synthesis



# Danishefsky's synthesis



# Danishefsky's synthesis



# Conclusion

- A perfect example of the old saying “There is more than one way to skin a cat.” (See *Org. Lett.* **2007**, 9, 2143-2146 for the latest total synthesis of *salinosporamide*.)

# References

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- Ling, T.; Macherla, V.; Manam, R.; McArthur, K.; Potts, B. *Org. Lett.*, **2007**, *9*, 2289-2292.
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- Corey, E. J.; Fournier, J.; Reddy, B.; Reddy, L. *Org. Lett.*, **2005**, *7*, 2699-2701.