

Synthesis of Azadirachtin:

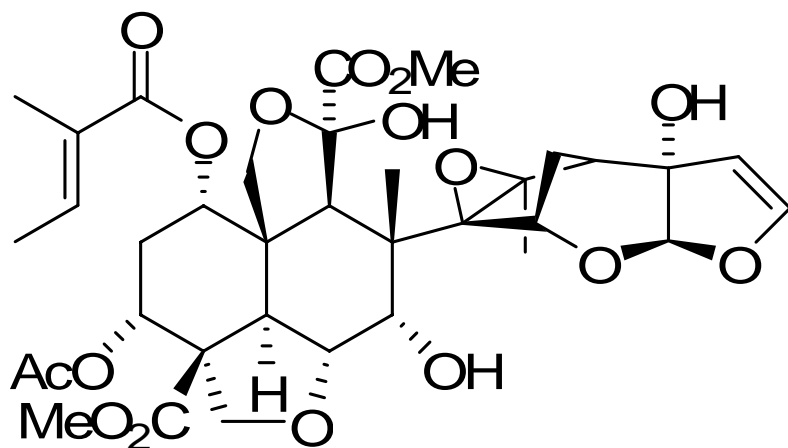
This synthesis is almost as old as I am.

Tim Martin

Group Meeting

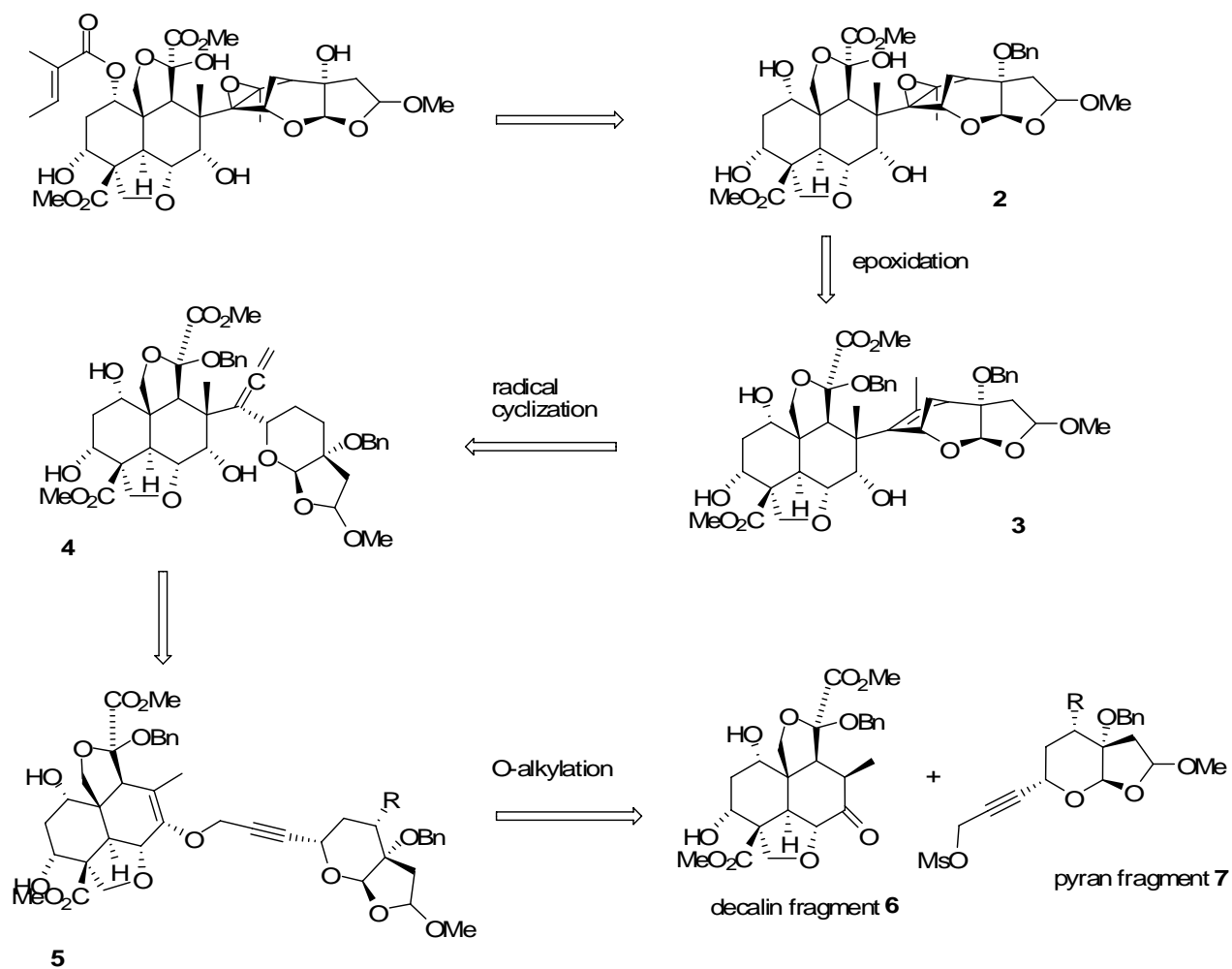
8/8/07

Structure

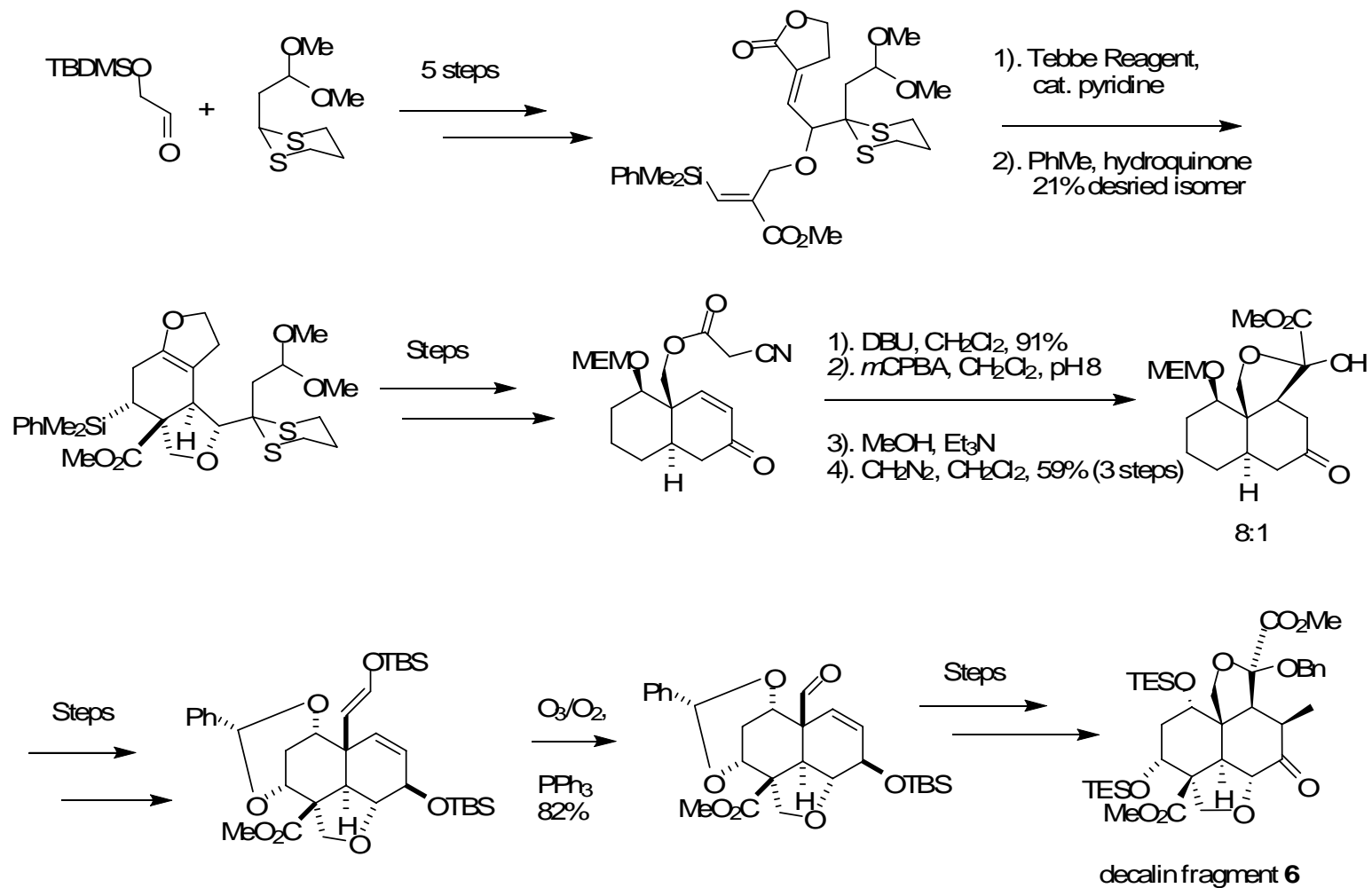


- Isolated from Indian neem tree, *Azadirachta indica*, in 1968
- Structure not elucidated until 1987
- 16 contiguous stereogenic centers, seven of which are quaternary centers
- Many oxygenated functionalities
- Rigid structure due to H-bonding

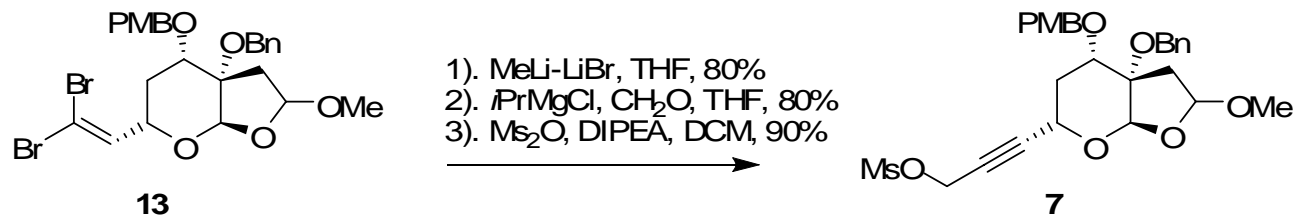
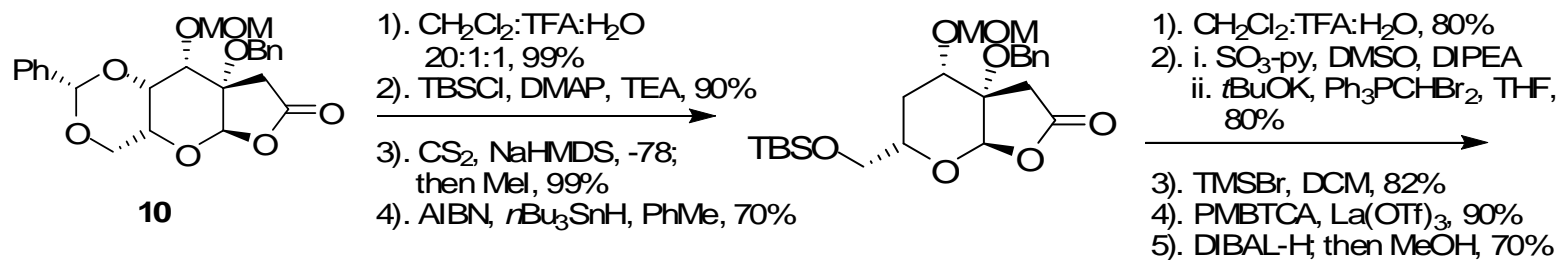
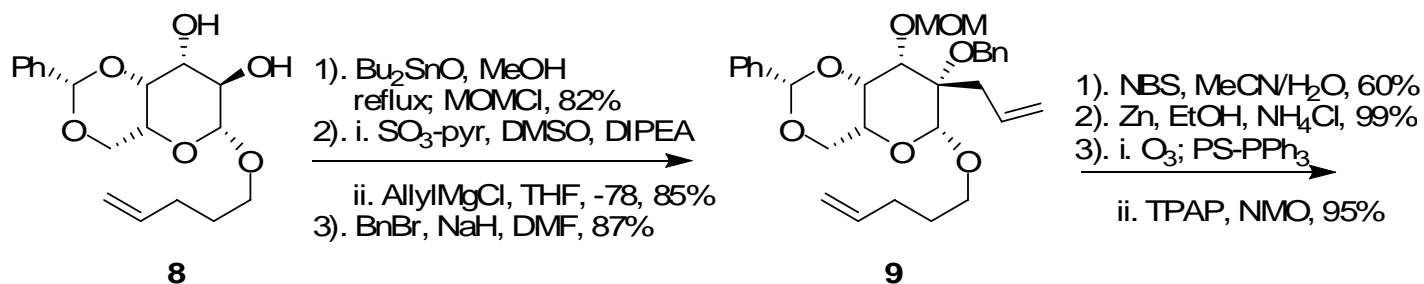
Ley's Retrosynthesis



Ley's Synthesis: Decalin 6



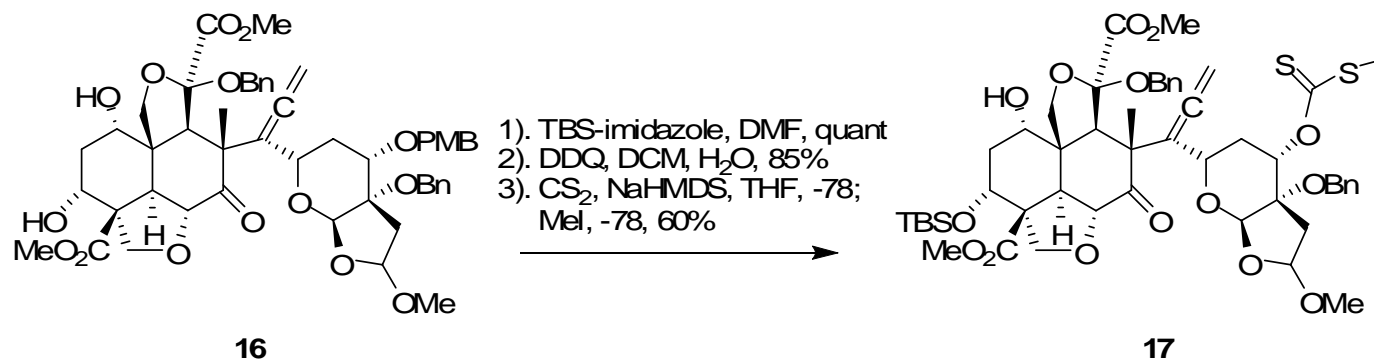
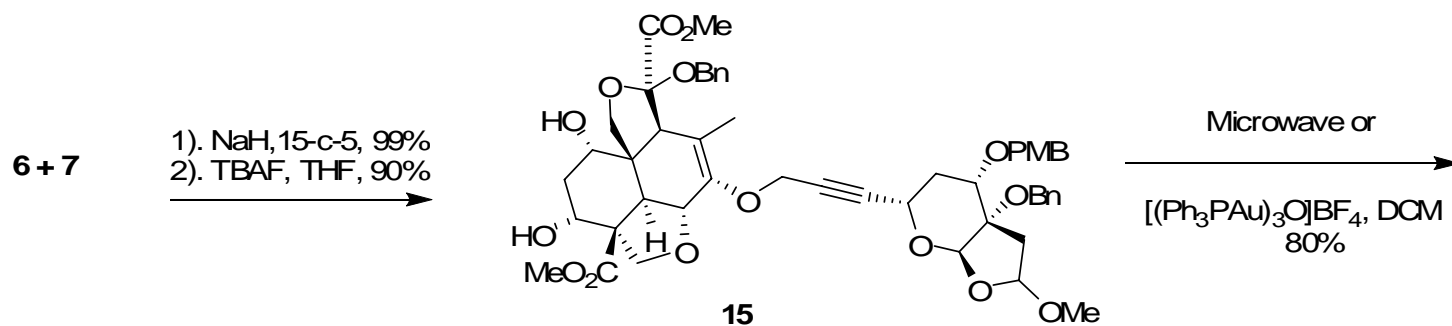
Ley's Synthesis: Pyran 7



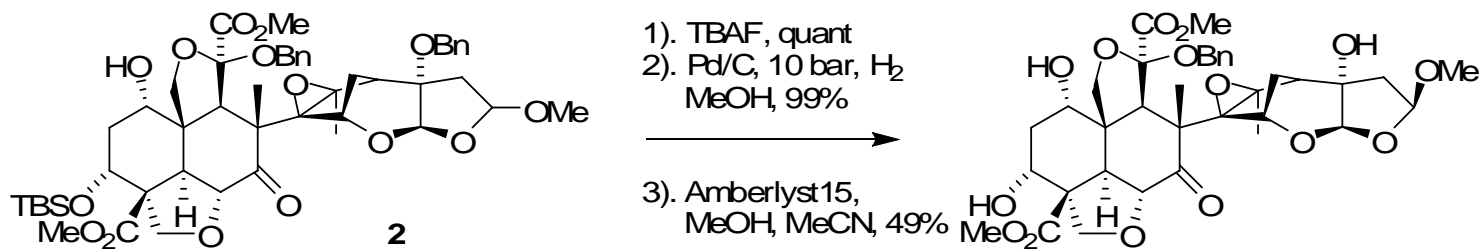
ACIE, 2007, 46

JACS, 1988, 110, 2663-4

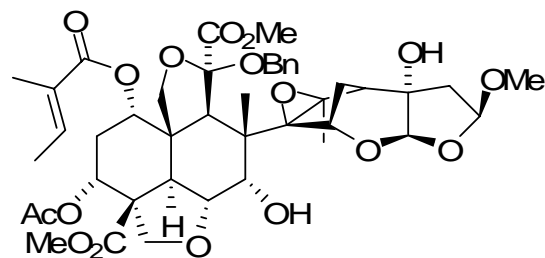
Ley's Synthesis



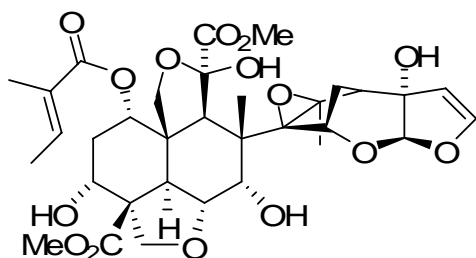
Ley's Endgame



- 1). Ac₂O, Et₃N, DMAP, 74%
- 2). CH₃CH₂(CH₃)(CO)O(CO)C₆H₂Cl₃,
Cs₂CO₃, toluene, reflux, 6 days,
50 (80% brsm)
- 3). NaBH₄, CeCl₃·7H₂O, MeOH, 49%

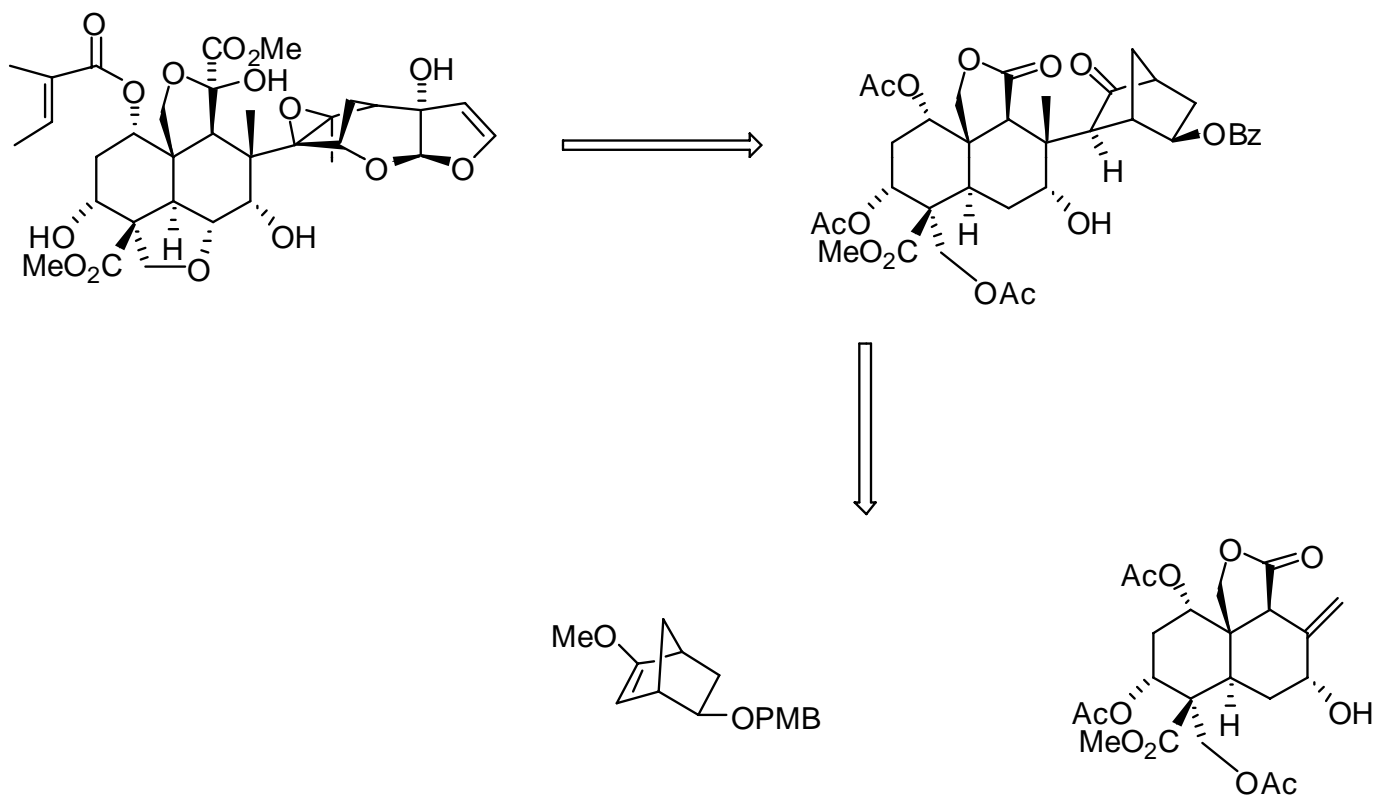


- 1). Pd/C, H₂, MeOH, rt, 81%
- 2). PhSH, PPTS, DCE, 70%
- 3). DMSO, DCM, -78 to rt,
then PhMe and reflux
67%

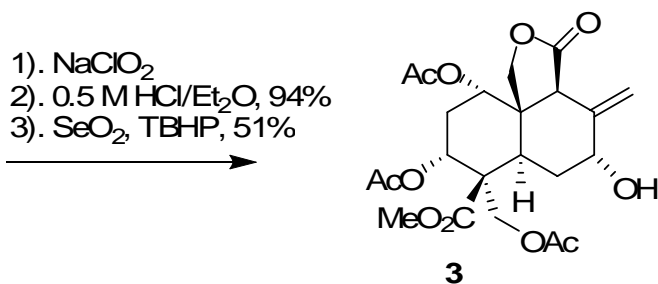
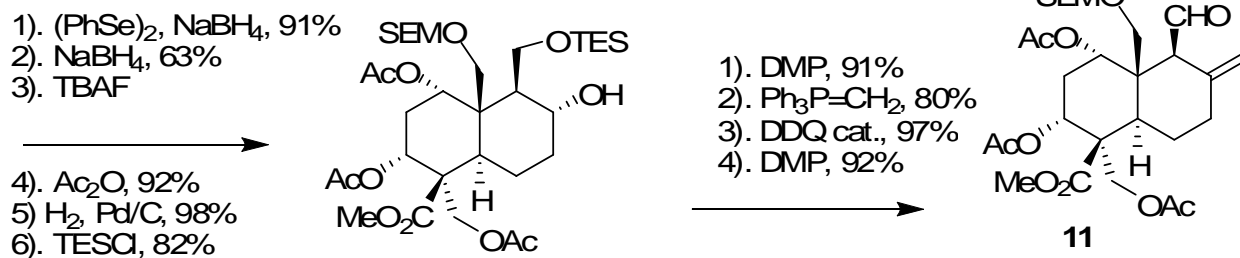
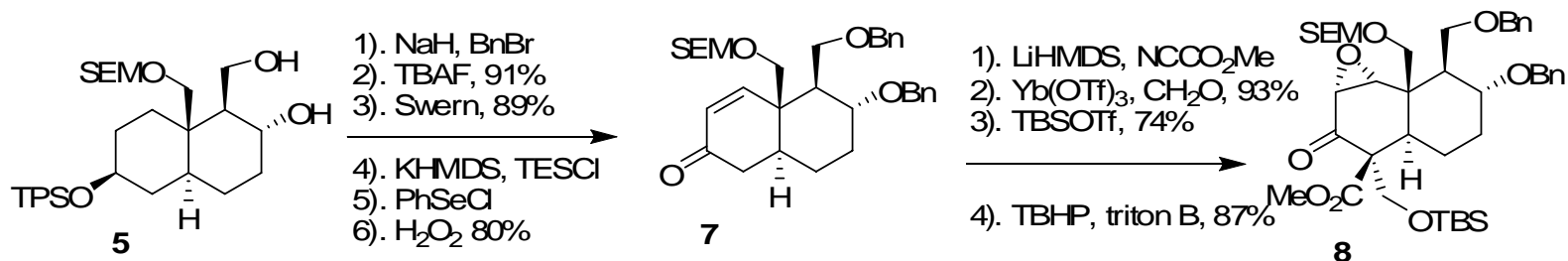


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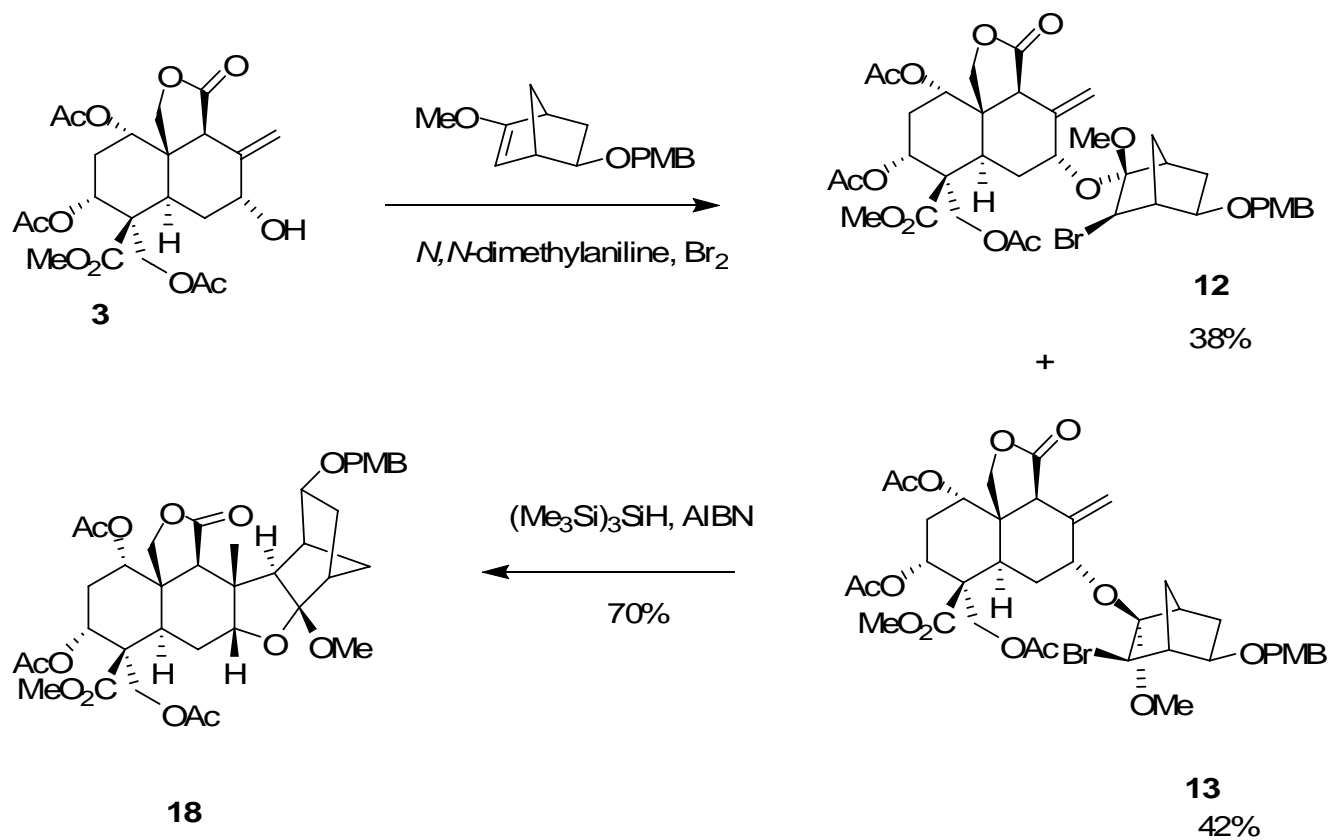
Nicolaou's Synthesis of the ABC Framework



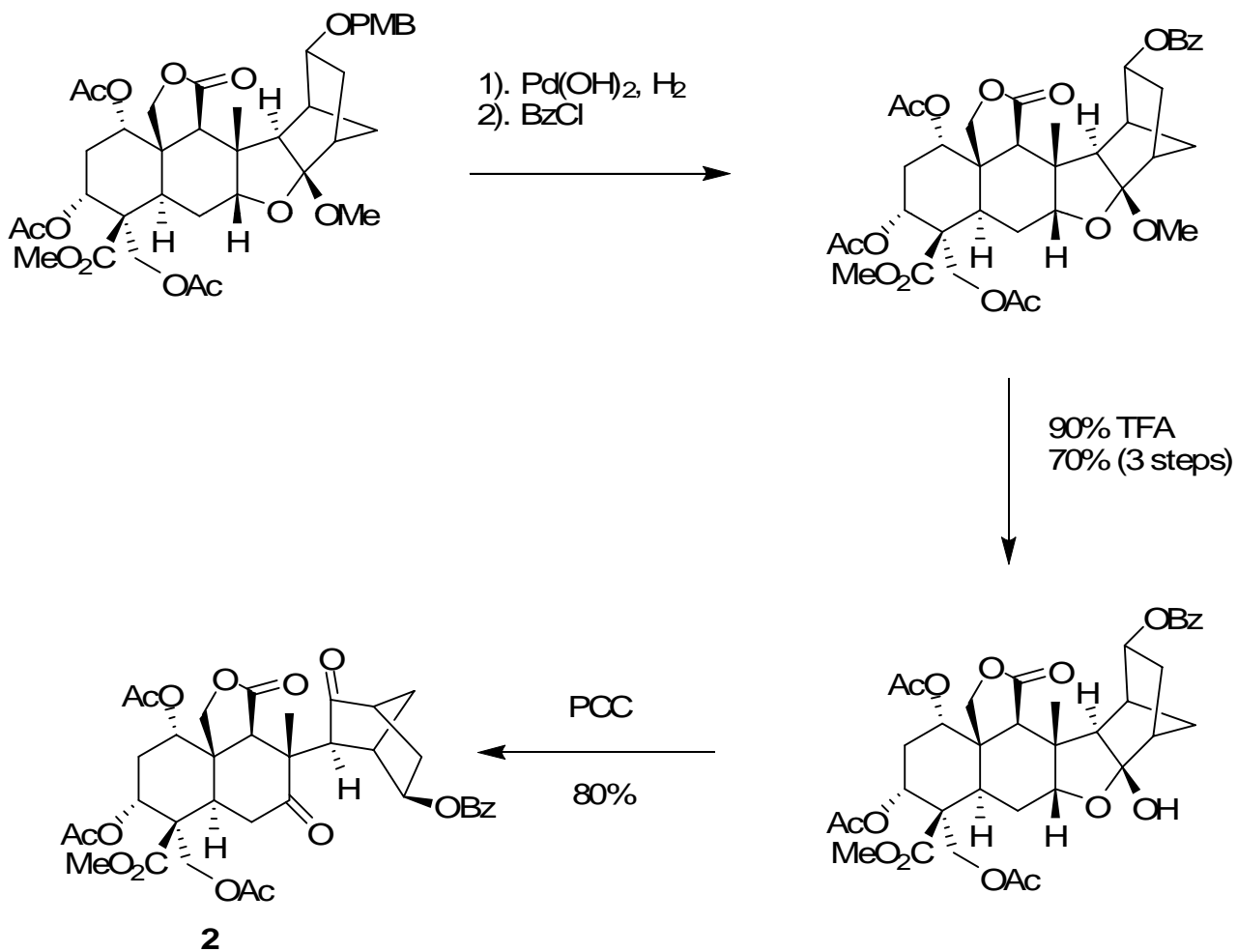
Nicolaou Synthesis: Decalin 3



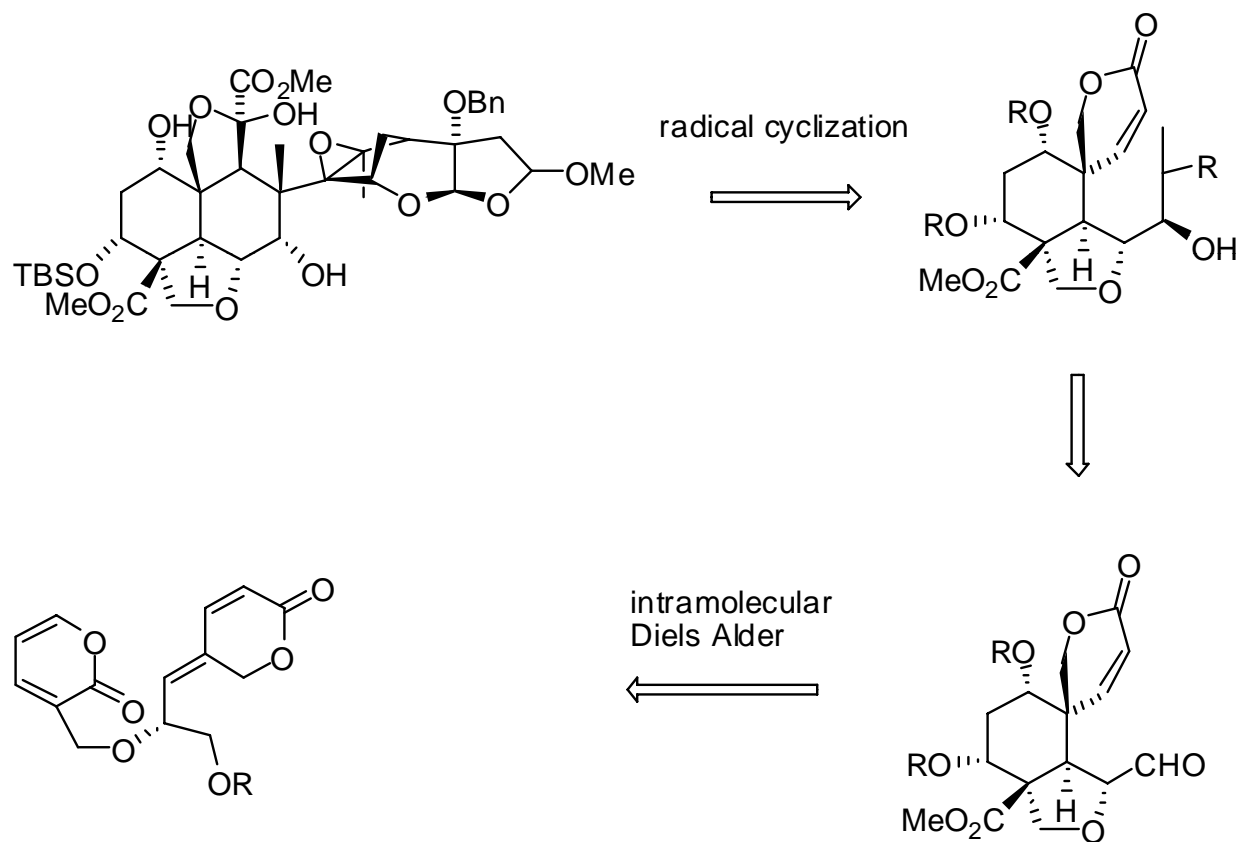
Nicolaou's Synthesis: Coupling



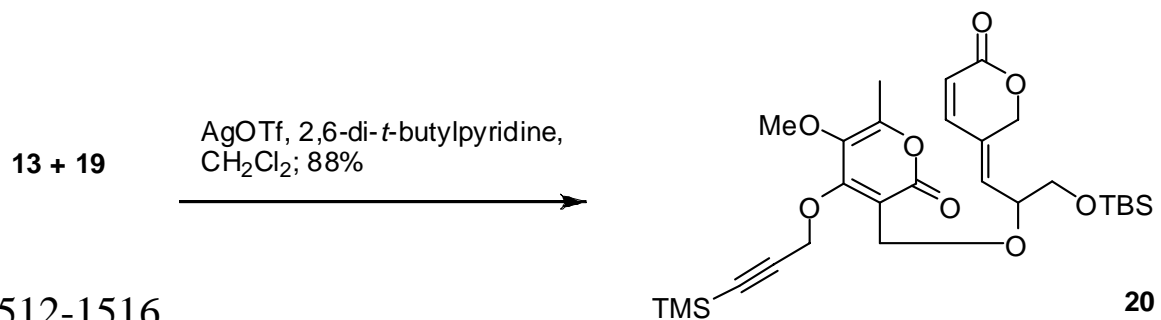
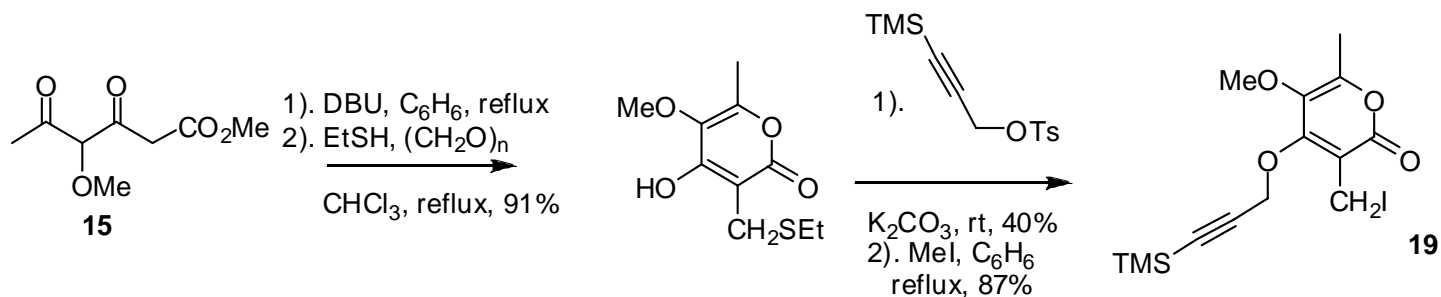
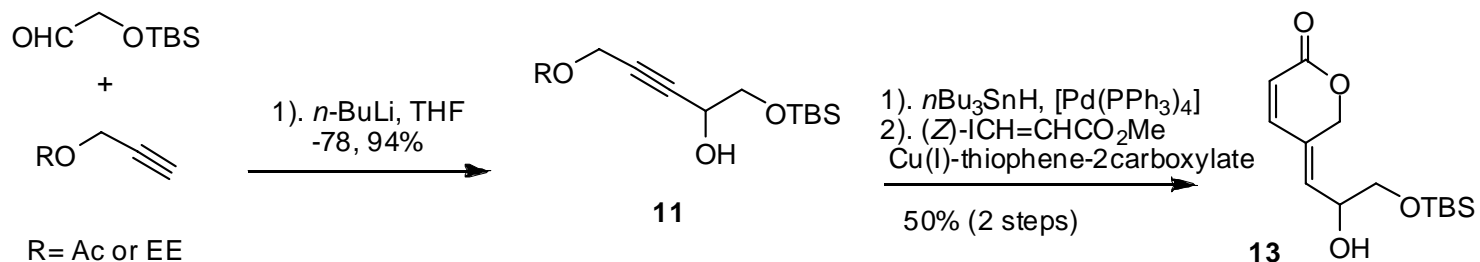
Nicolaou's Synthesis: Azadirachtin Precursor



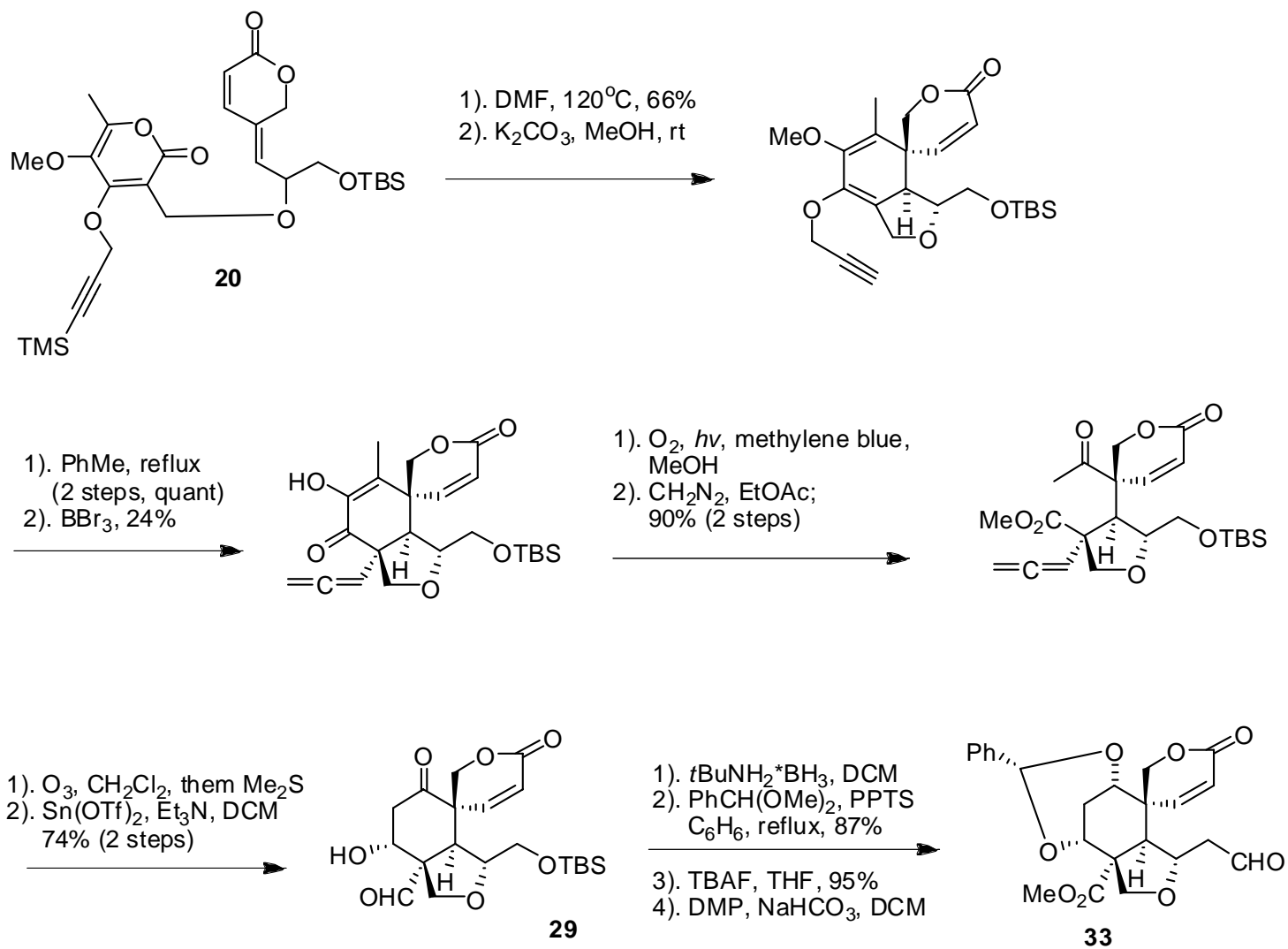
Watanabe's Synthesis of the AB rings



Watanabe's Synthesis: IMDA precursor



Synthesis of the “Left-Hand Segment”



Watanabe: Synthesis of 2

