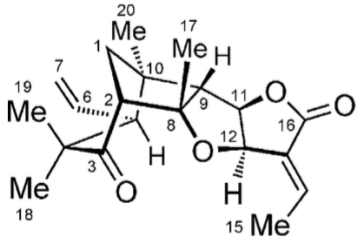
Protecting-Group-Free Enantioselective Synthesis of (-)-Pallavicinin and (+)-Neopallavicinin

Huang, B., Guo, L., Jia, Y., ACIE **2015**, 54, 13599-13603

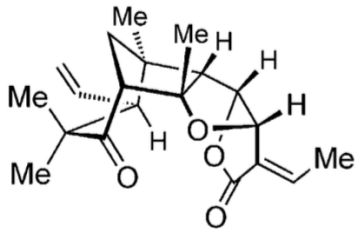
Wipf Group Current Literature 11-21-15
James Johnson

Pallavicinins

- Isolated from Asian Liverworts (bryophytes) *Pallavicinia subciliata* and *P. ambigua*
- Structures determined by X-ray diffraction and CD analysis.
- Contains a novel cagelike 6-5-5-5 tetracyclic skeleton with seven contiguous stereocenters
- Bioactivities include antipyretic properties, muscle regeneration, and detoxification
- Other similar diterpenoids exhibit 10 μM activity towards leukemic K562/A02 cells.
- Only one example: (±) Pallavicinin and (±) Neopallavicinin (32 steps 0.1% and 0.007% overall yield)



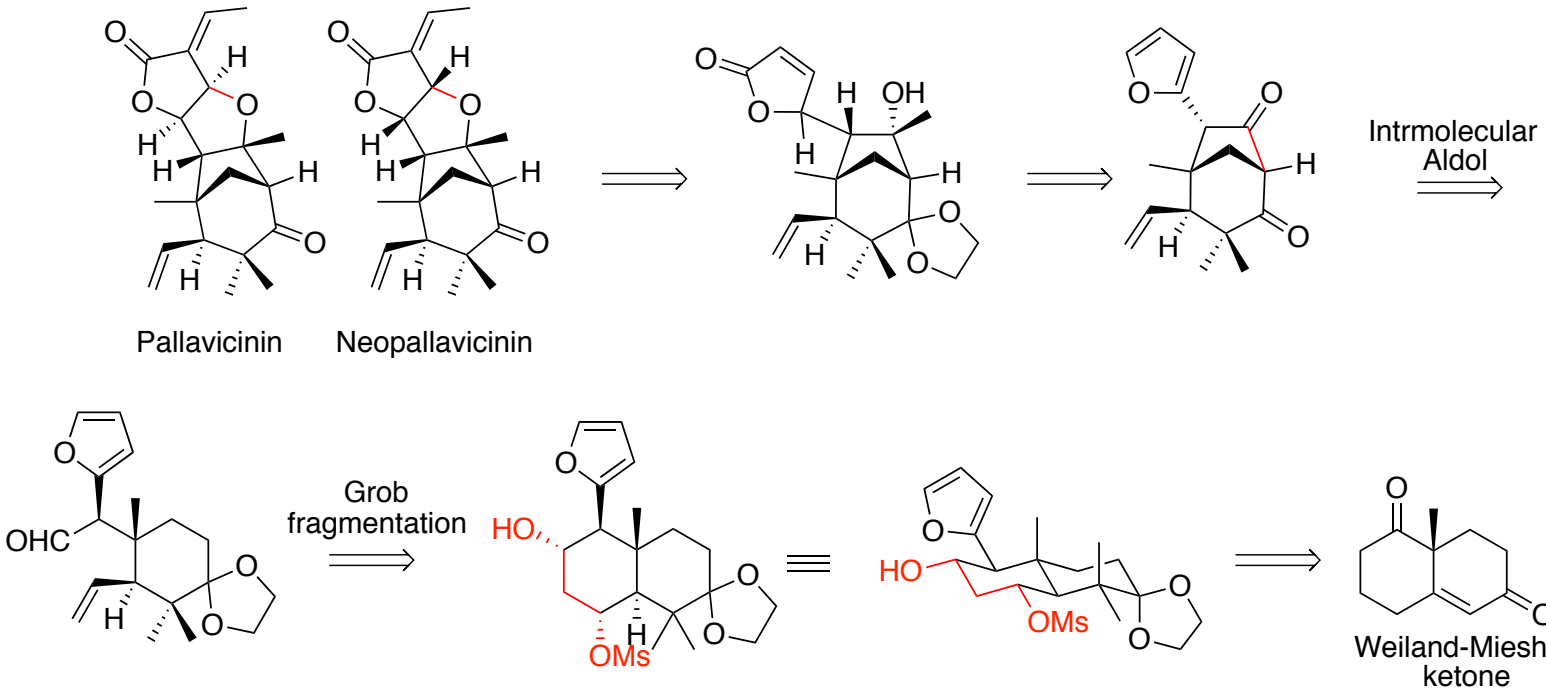
(–)-pallavicinin [(–)-**1**]



(+)-neopallavicinin [(+)-**2**]

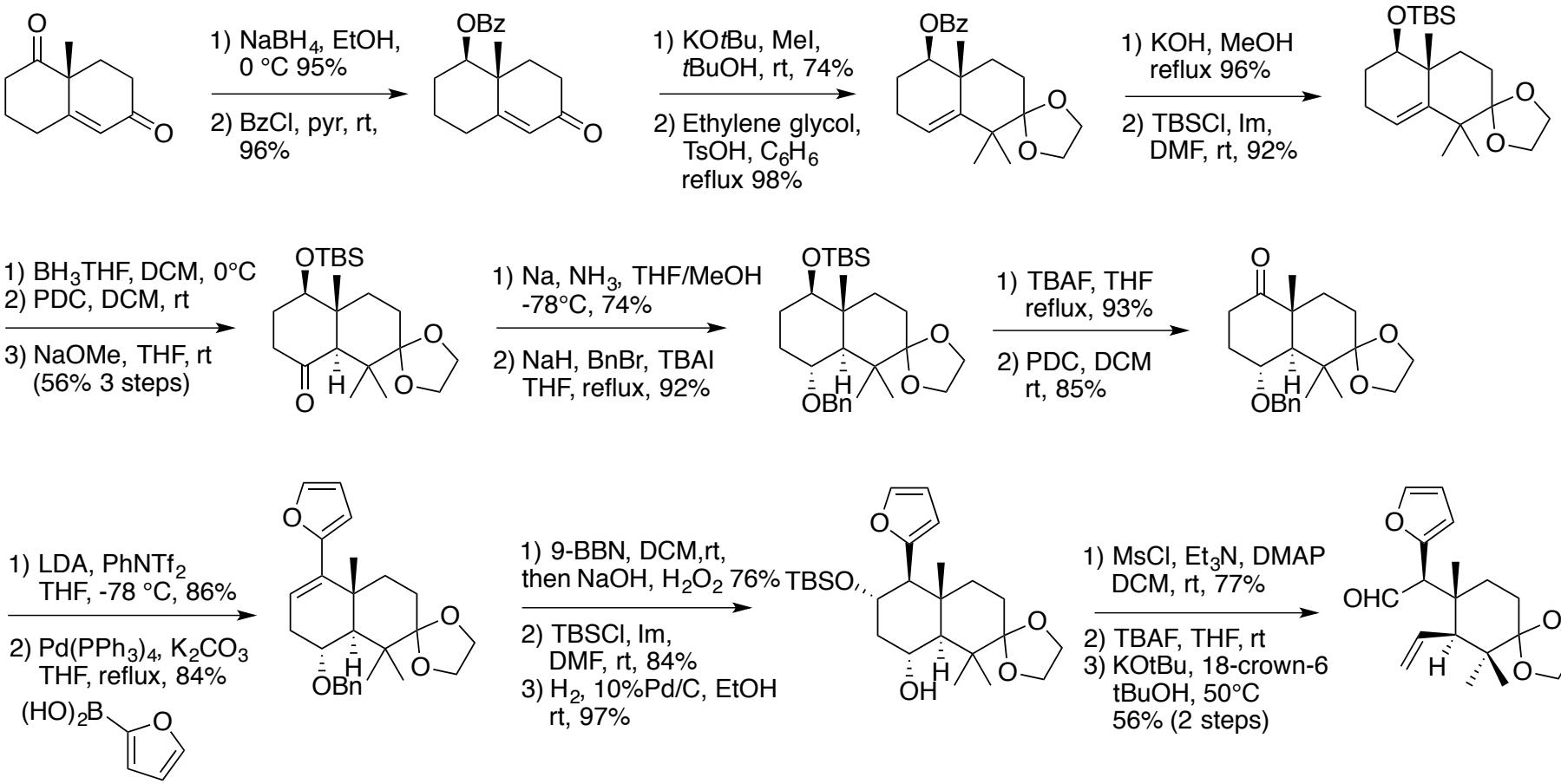
Chem. Asian J. 2006, 1, 111
Chem. Pharm. Bull. 1998, 46, 178

Wong's Biomimetic Synthesis



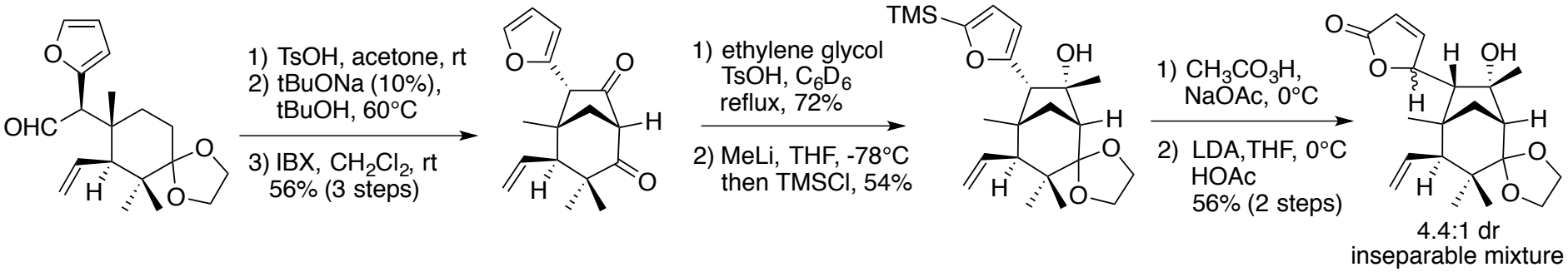
Chem. Asian J. 2006, 1, 111

Wong's Biomimetic Synthesis



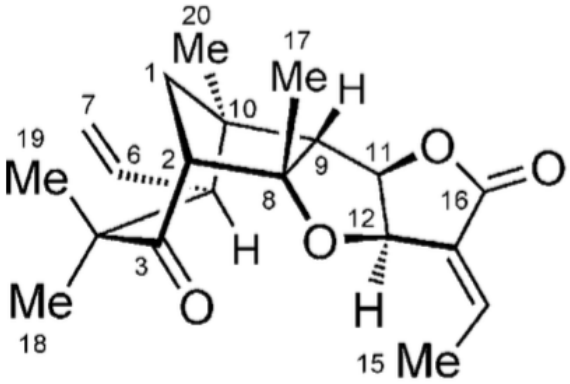
Chem. Asian J. 2006, 1, 111

Wong's Biomimetic Synthesis

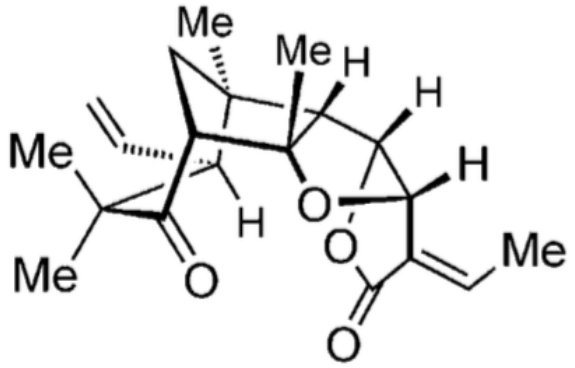


Chem. Asian J. **2006**, 1, 111

Title Paper

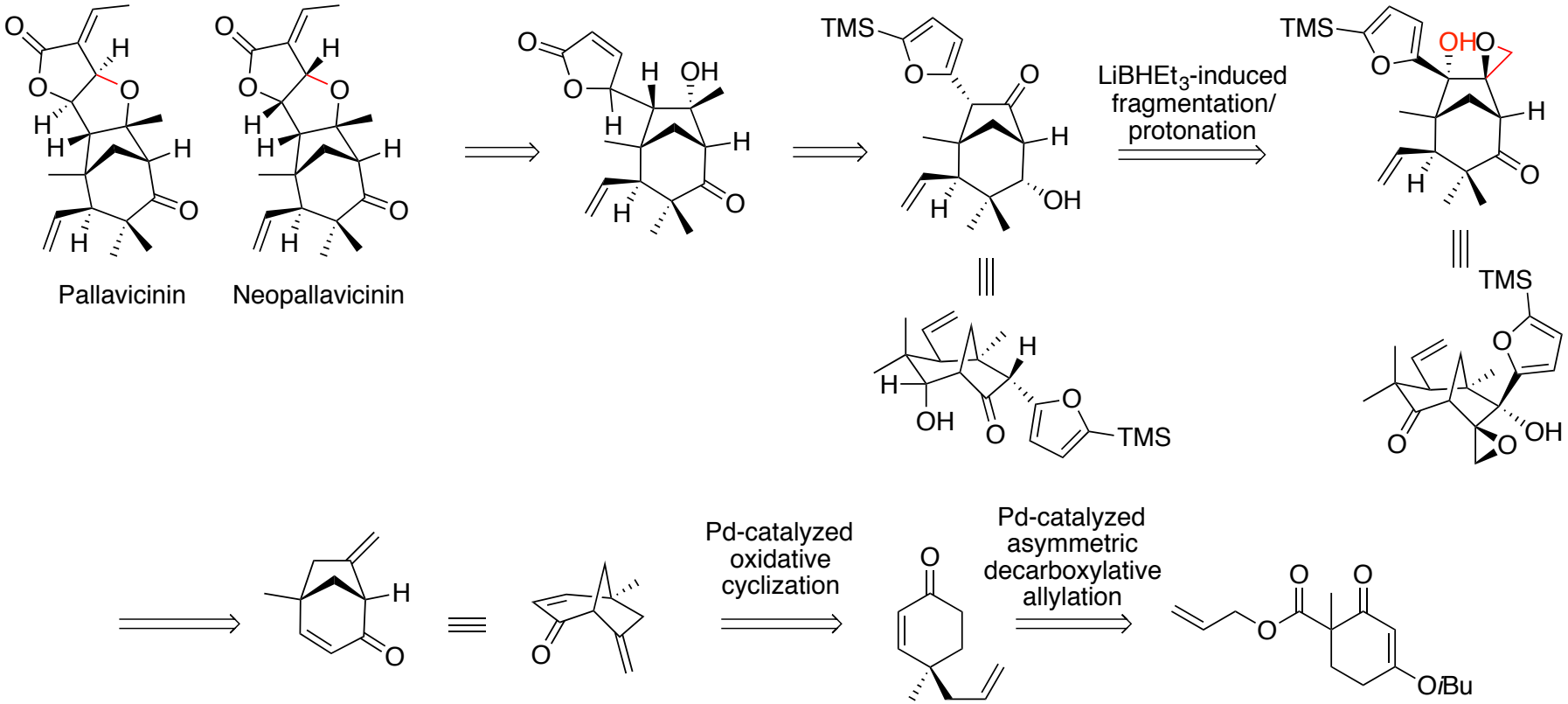


(–)-pallavicinin [(–)-**1**]



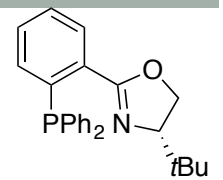
(+)-neopallavicinin [(+)-**2**]

Retrosynthesis

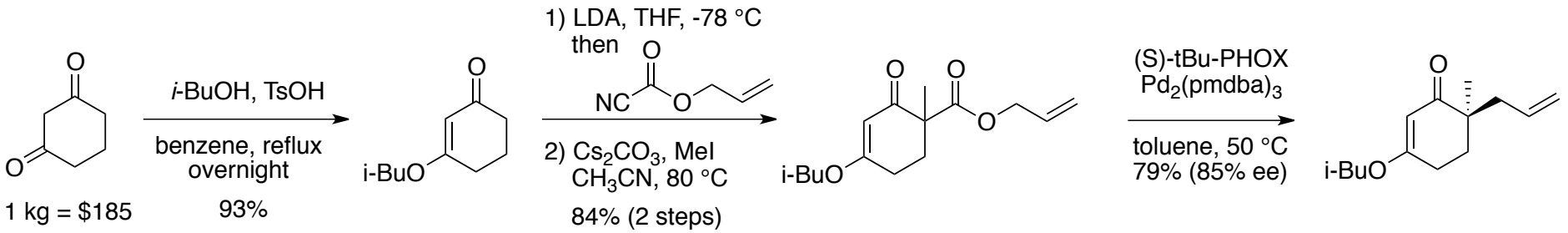


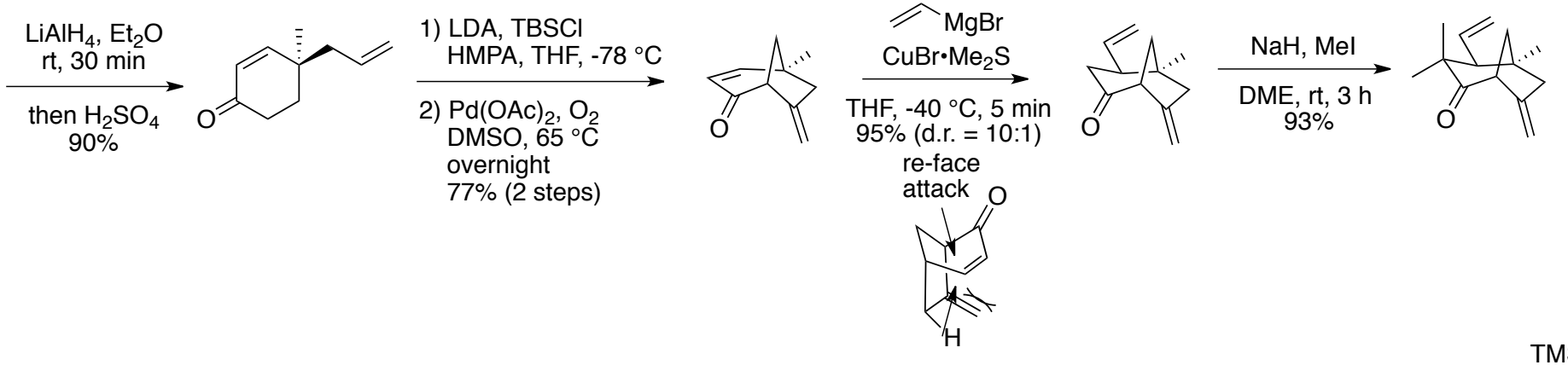
ACIE, **2015**, 54, 13599-13603

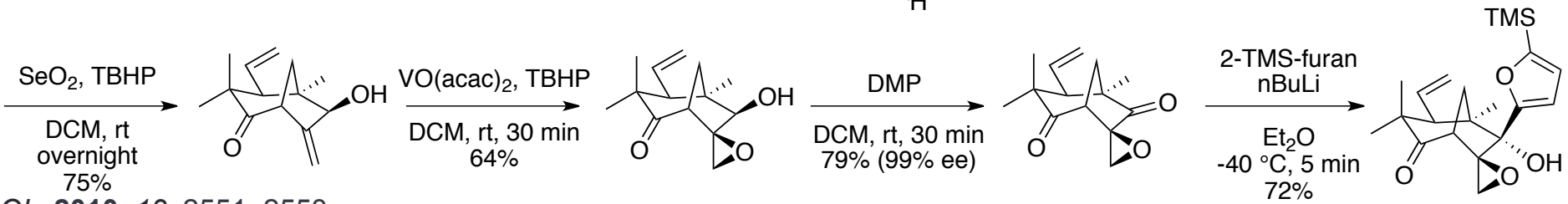
Synthesis of Payne Precursor



(S)-*t*Bu-PHOX

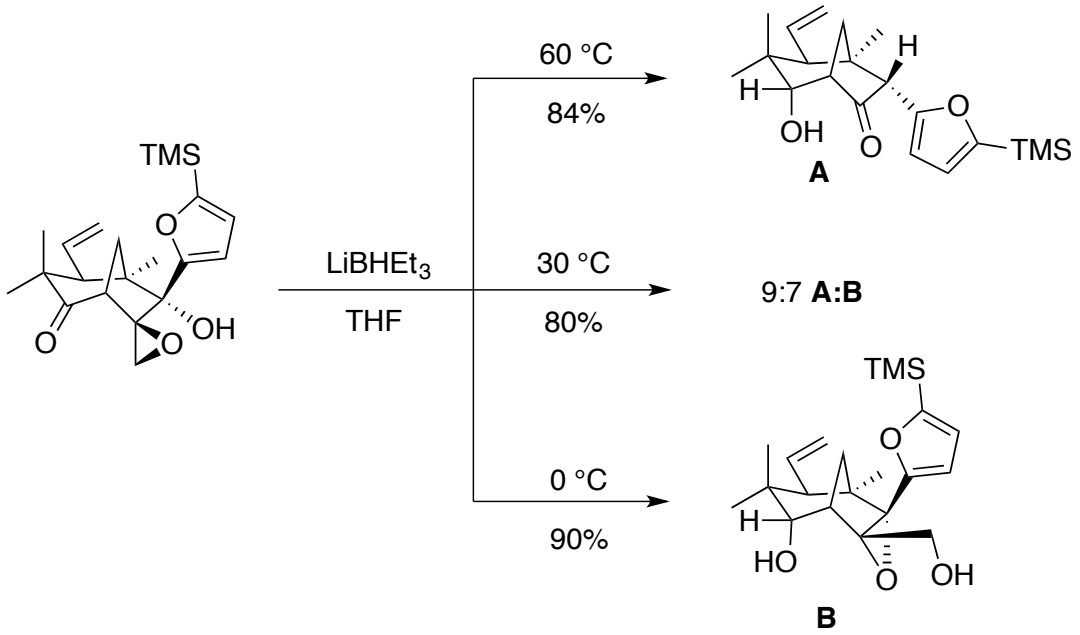


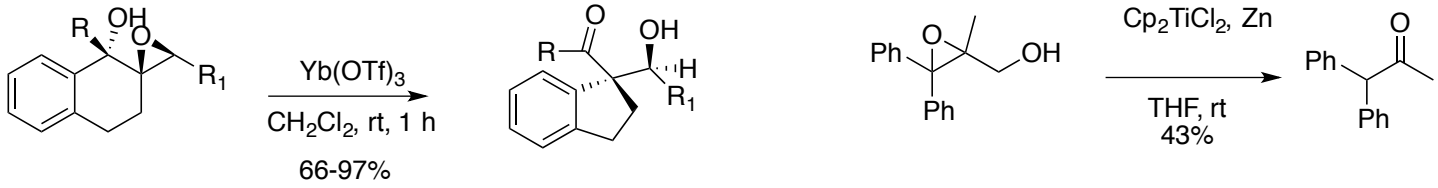




OL. **2010**, *12*, 2551–2553
ACIE, **2011**, 50, 2756-2760
ACIE, **2015**, 54, 13599-13603

$LiBHEt_3$-mediated Payne rearrangement





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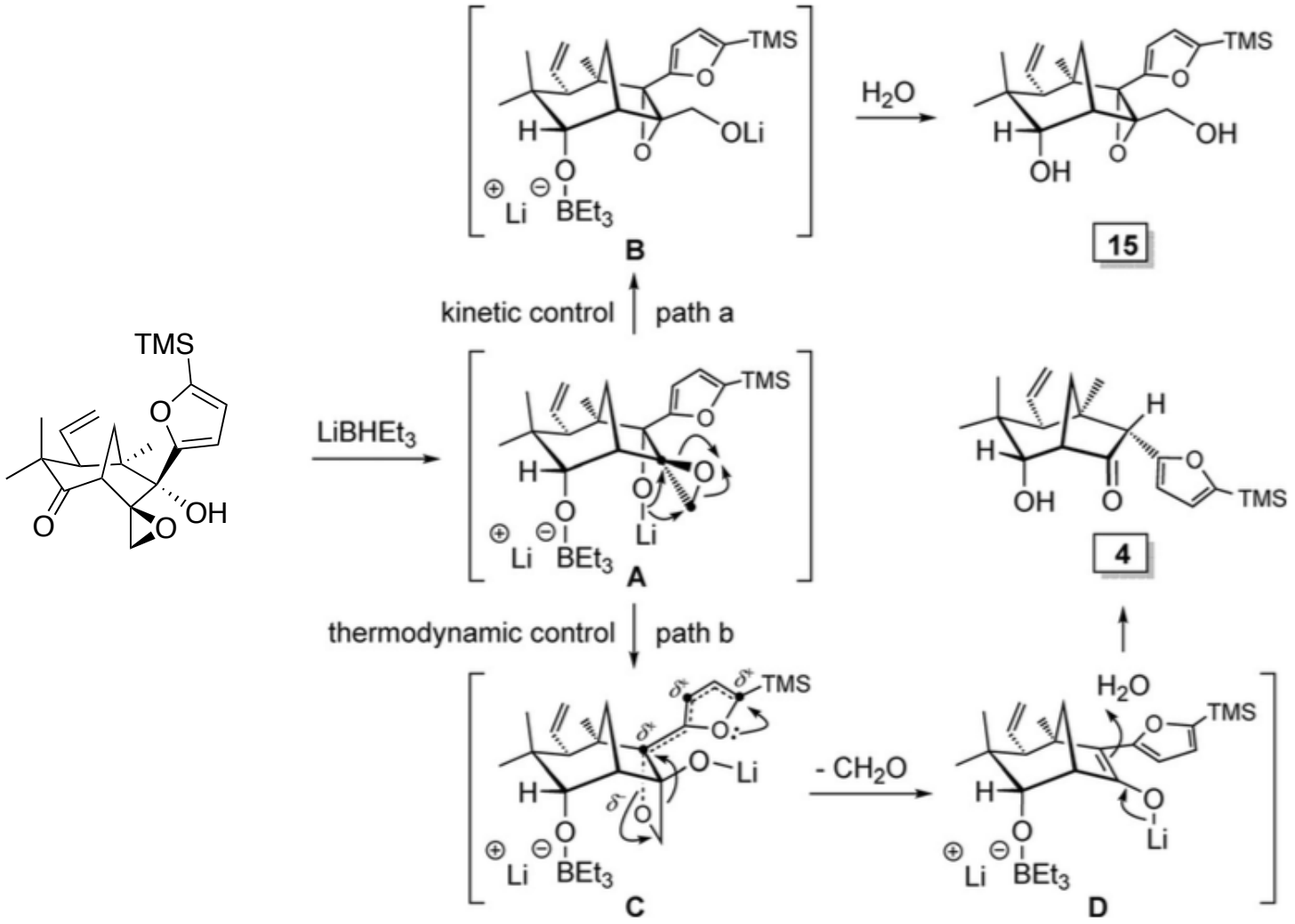
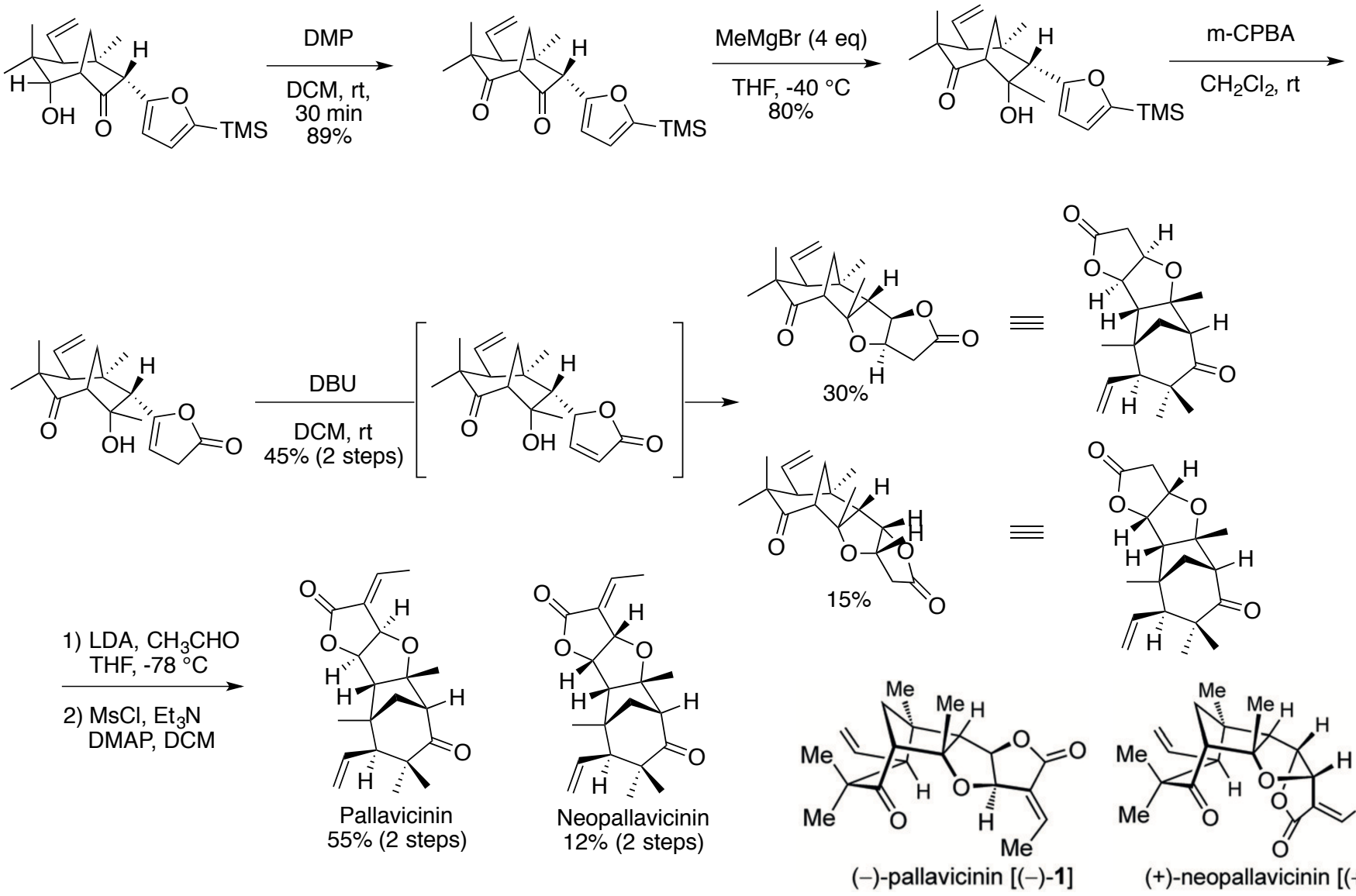
Proposed Mechanism



The Final Steps



Conclusions

- Protecting group free asymmetric synthesis of (-)-pallavicinin and (+)-neopallavicinin
- 15 steps. 1.3% and 0.1% for (-)-pallavicinin and (+)-neopallavicinin from known compound. Improved from previous synthesis.
- New example of a $LiBHEt_3$ induced “Payne” rearrangement