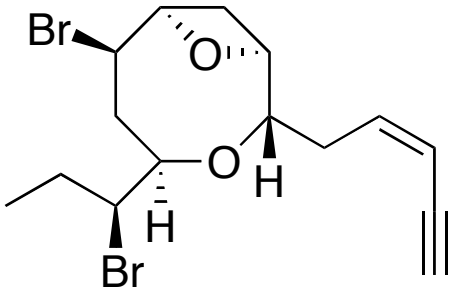
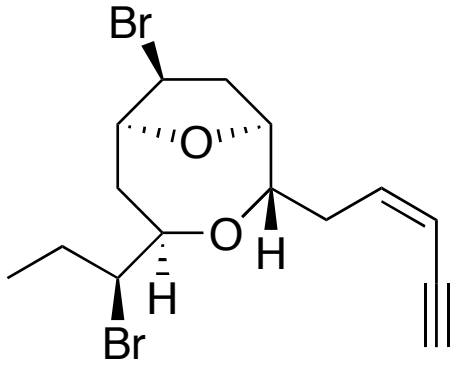
Asymmetric Total Syntheses of (+)-3-(*Z*)-Laureatin and (+)-3-(*Z*)-Isolaureatin by "Lone Pair-Lone Pair Interaction-Controlled" Isomerization

Hyoungsu Kim, Hyunjoo Lee, Dongjoo Lee, Sanghee Kim, and Deukjoon Kim;

J. Am. Chem. Soc. ASAP



(+)-3-(*Z*)-Laureatin



(+)-3-(*Z*)-Isolaureatin

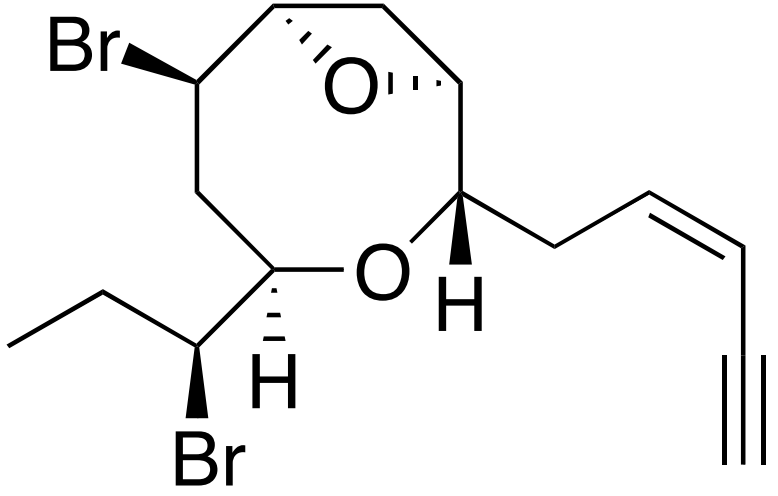
Adam Hoye

Current Literature

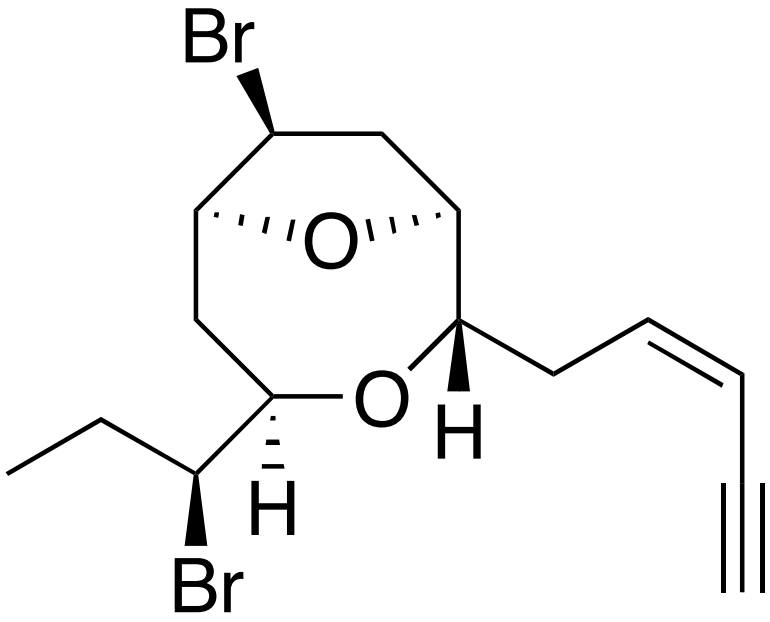
Feb. 17, 2007

Wipf Group

Structural Features



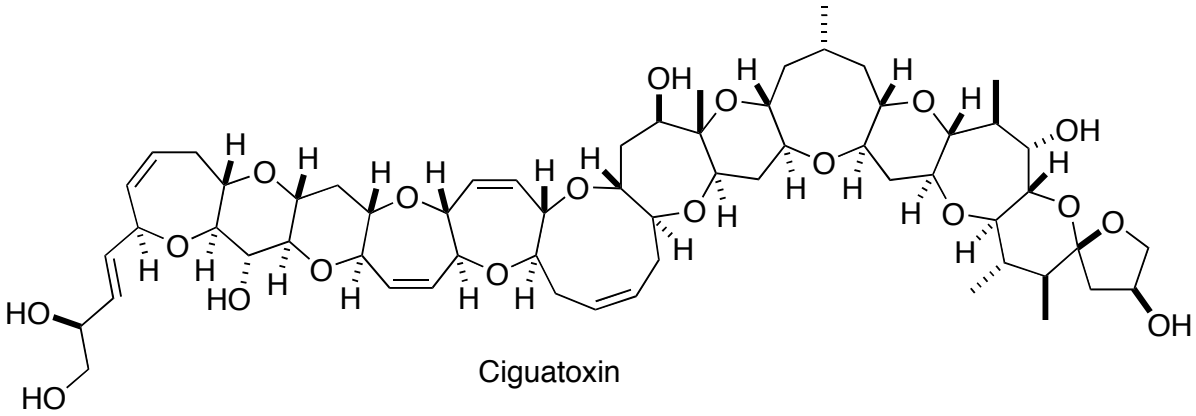
(+)-3-(*Z*)-Laureatin



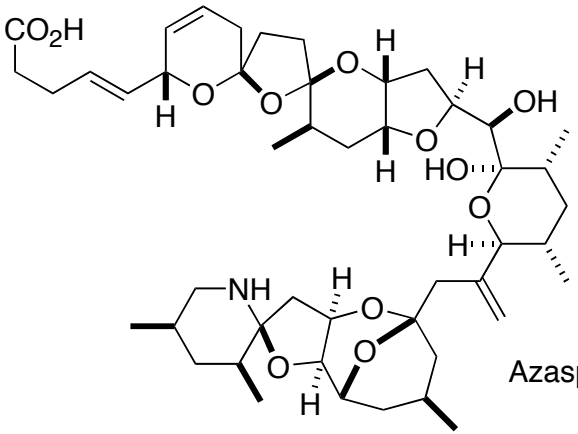
(+)-3-(*Z*)-Isolaureatin

- Dioxabicyclic ring system (medium-sized oxocene and oxetane/oxolane
- α, α'-*trans* relationship (6 stereocenters total)
- (*Z*)-enyne sidechain
- chiral halogen atoms

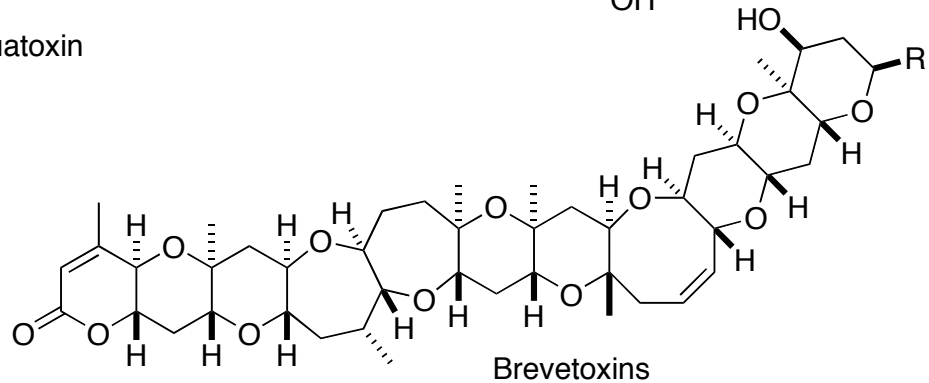
8-Membered Ring Ethers



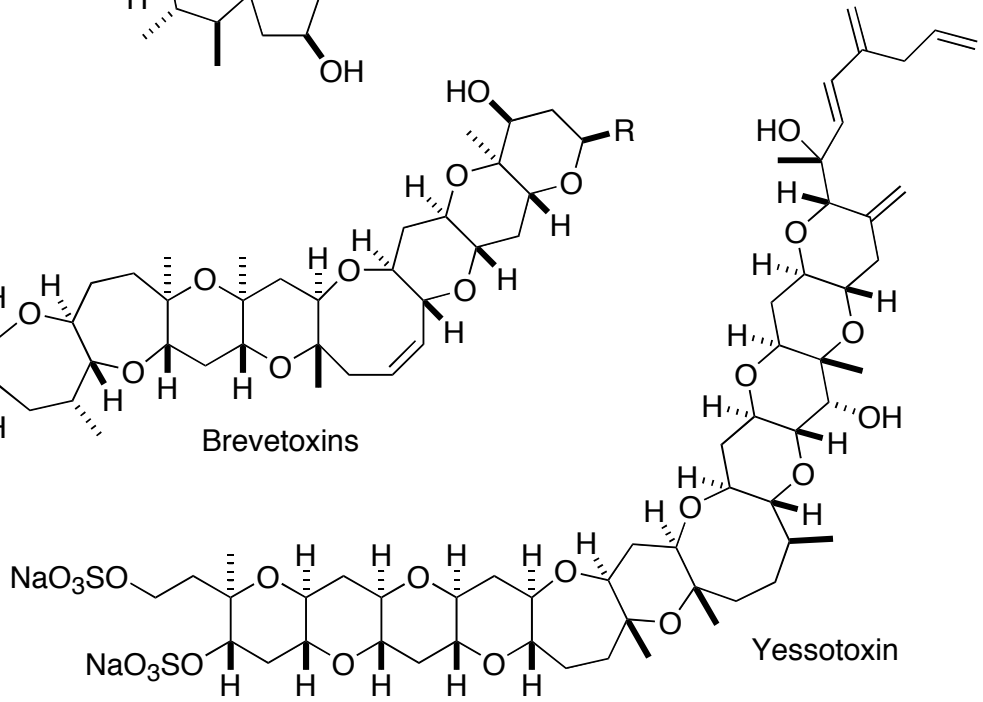
Ciguatoxin



Azaspiracid



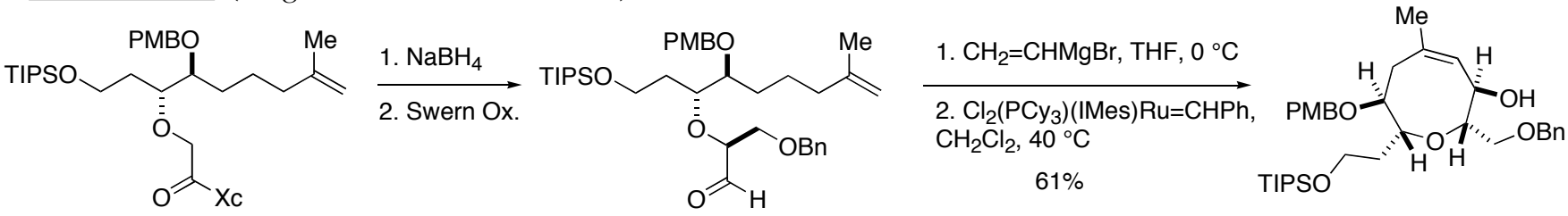
Brevetoxins



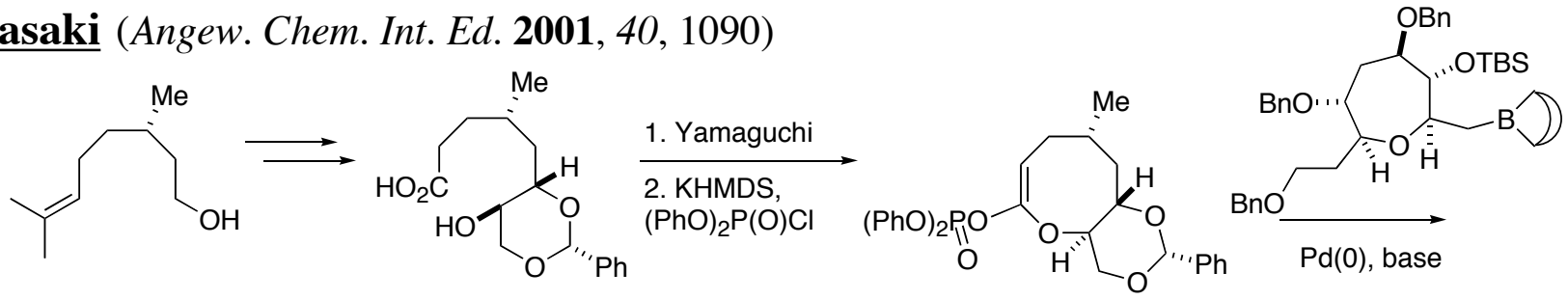
Yessotoxin

Construction of 8-Membered Ring Ethers

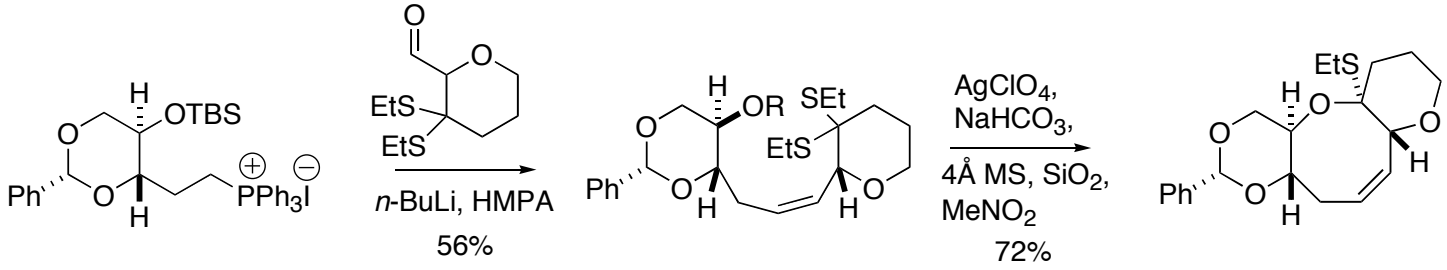
Crimmins (*Org. Lett.*, **2006**, *8*, 4079)



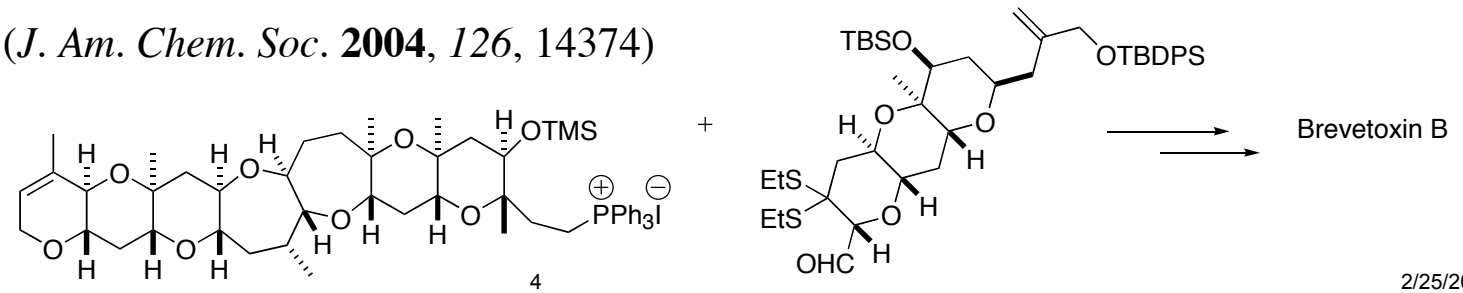
Sasaki (*Angew. Chem. Int. Ed.* **2001**, *40*, 1090)



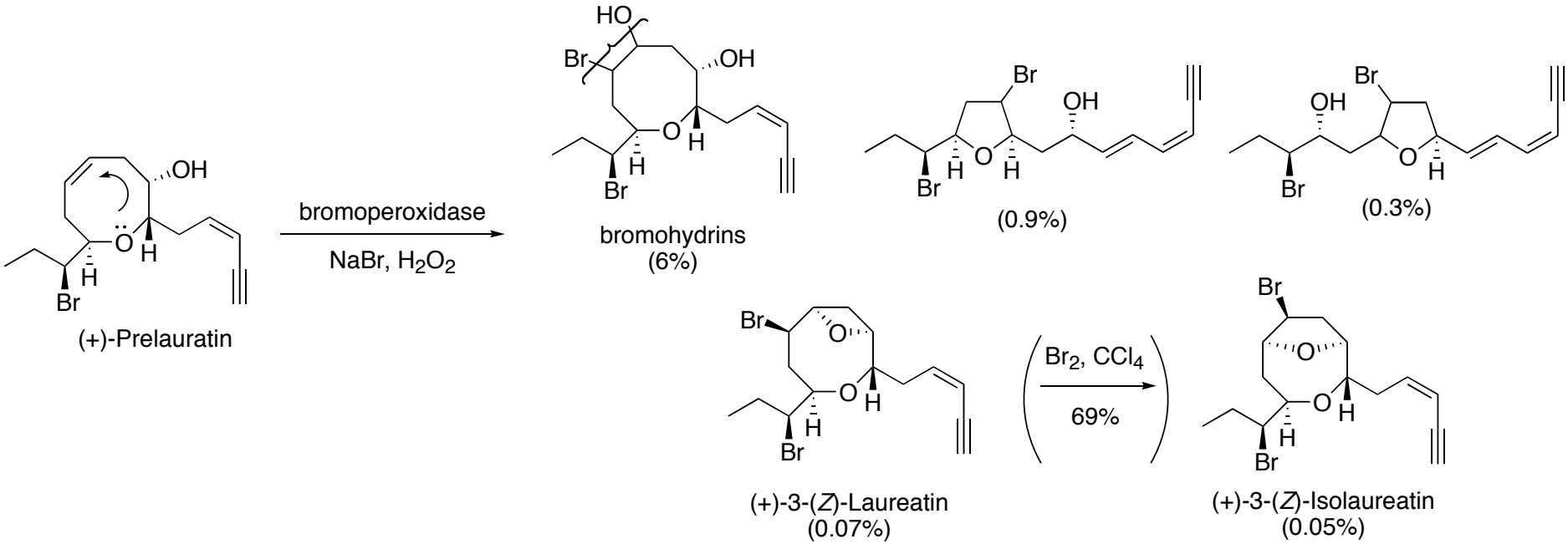
Nicolaou (*J. Am. Chem. Soc.* **1997**, *119*, 8105)



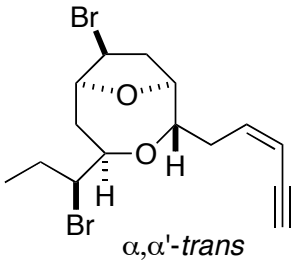
Nakata (*J. Am. Chem. Soc.* **2004**, *126*, 14374)



Enzymatic Study

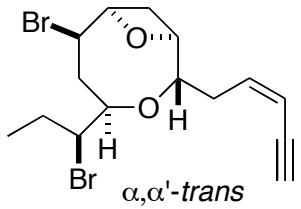


Retrosynthetic Plan



α,α'-*trans*

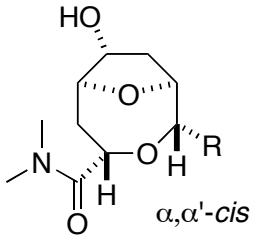
(+)-3-(*Z*)-Isolaureatin



α,α'-*trans*

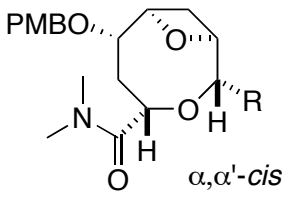
(+)-3-(*Z*)-Laureatin

Halogenation
&
"Lone Pair-Lone Pair
Interaction-
Controlled"
Epimerization
&
CM



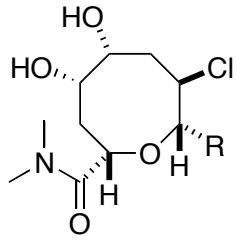
α,α'-*cis*

R= OBn

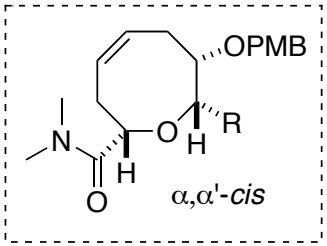


α,α'-*cis*

Williamson

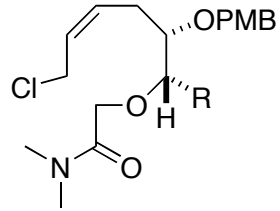


Halogenation
&
Osmylation

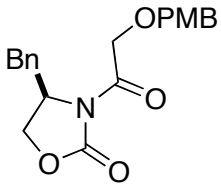


α,α'-*cis*

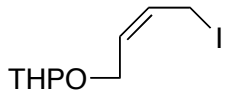
Intramolecular Amide
Enolate Alkylation

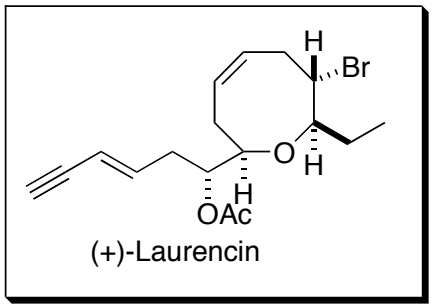


Evans



+

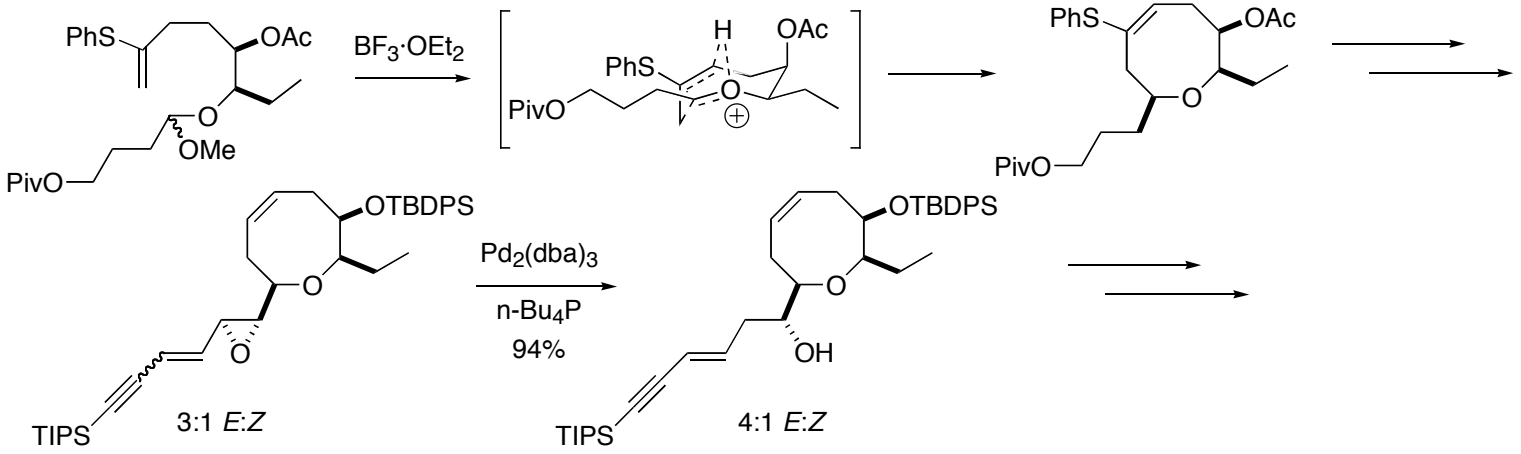




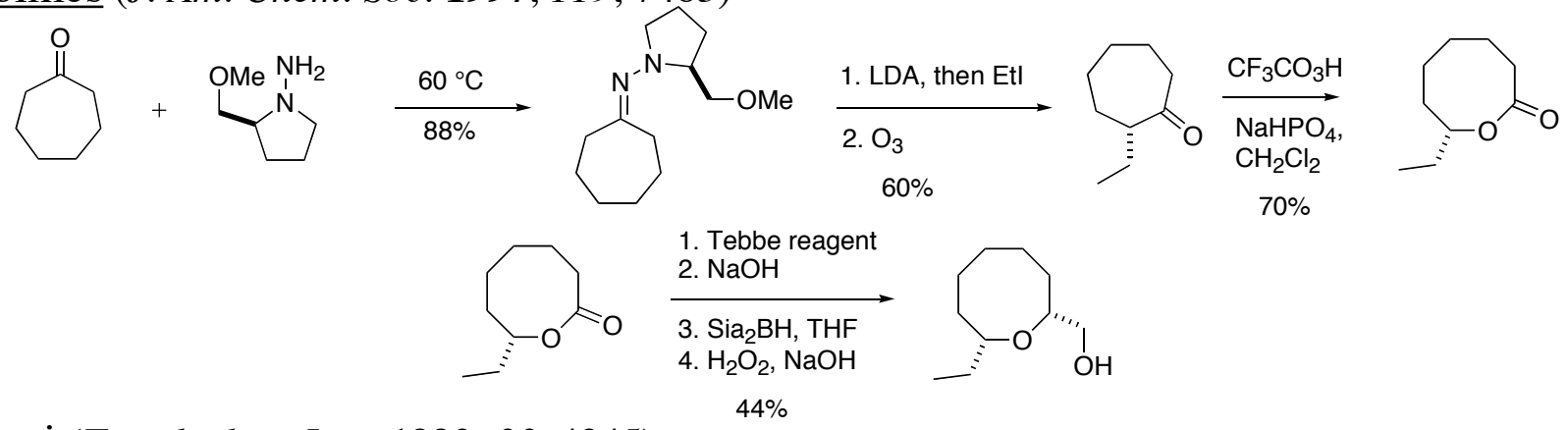
(+)-Laurencin

Laurencin Syntheses

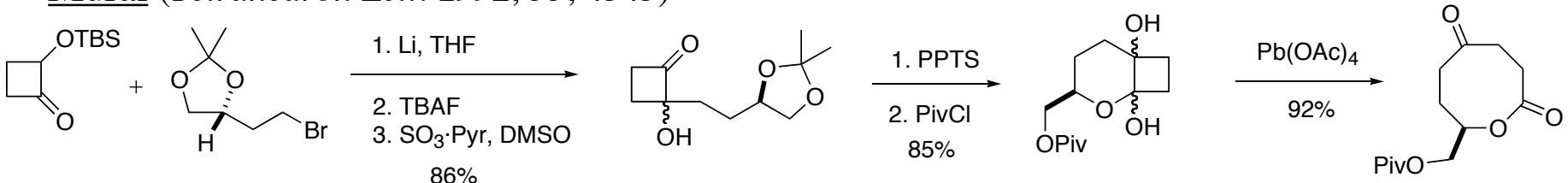
Overman (*J. Am. Chem. Soc.* **1995**, *117*, 5958)



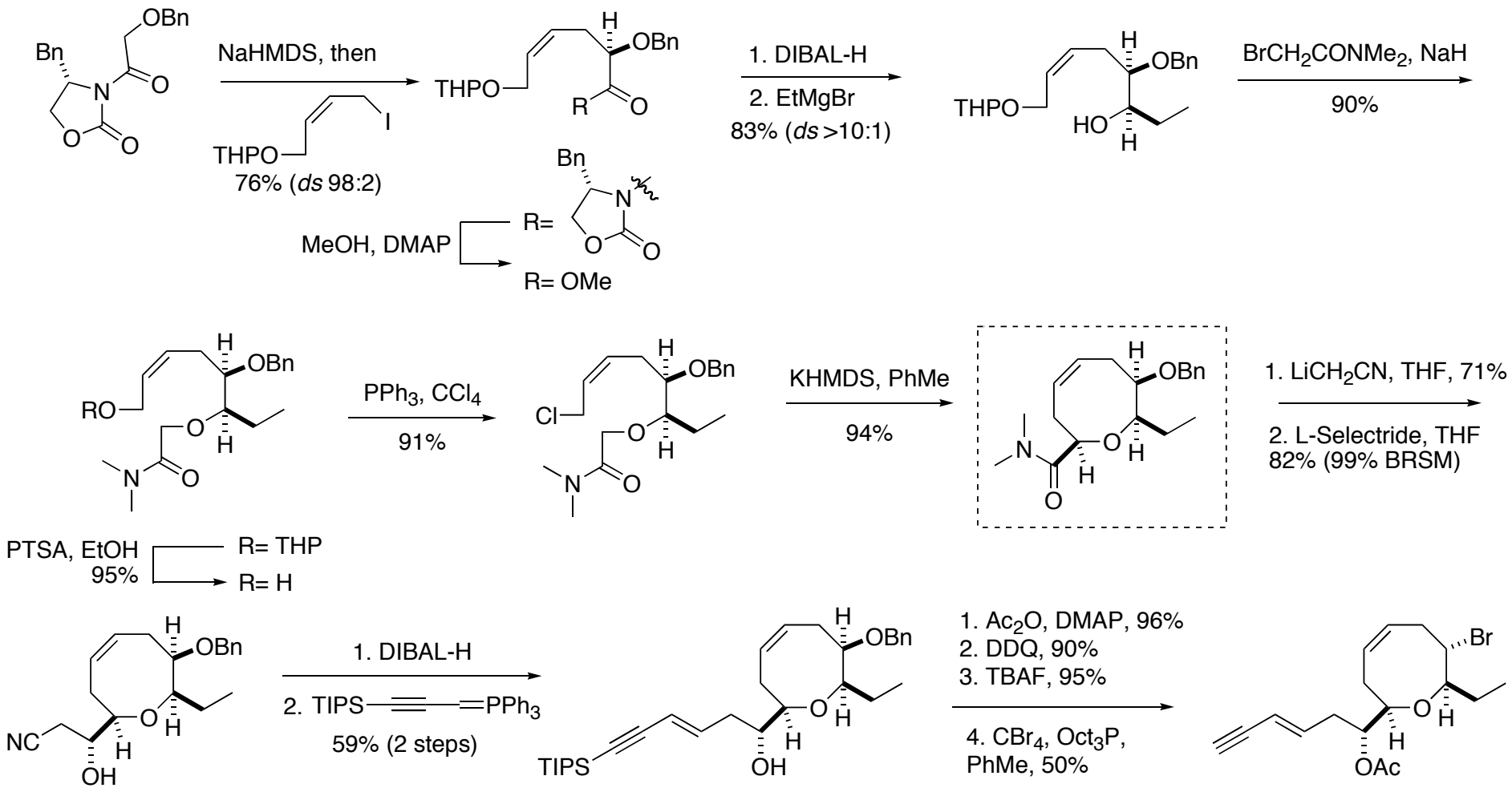
Holmes (*J. Am. Chem. Soc.* **1997**, *119*, 7483)



Murai (*Tetrahedron Lett.* **1992**, *33*, 4345)

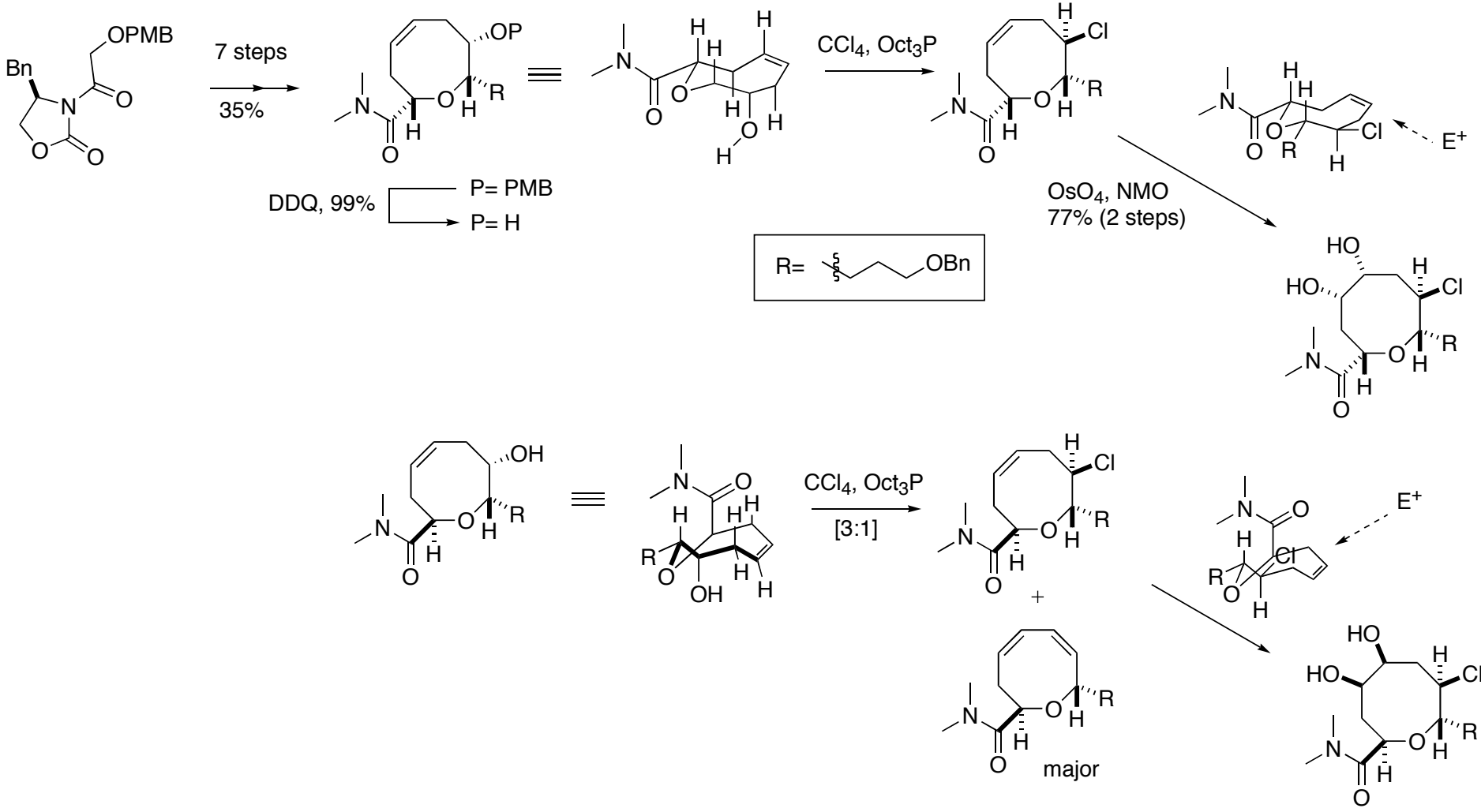


Kim Laurencin

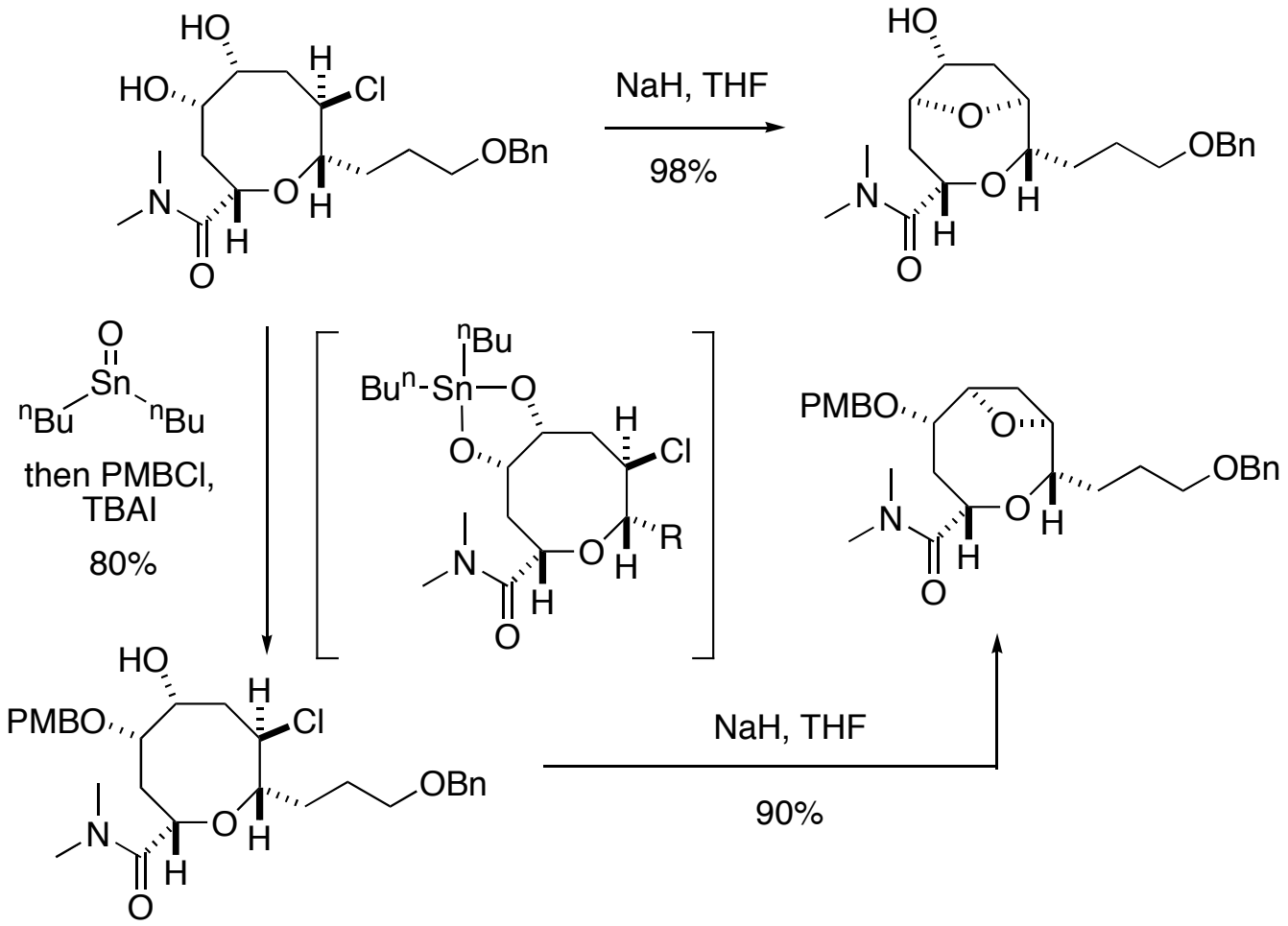


Baek, S.; Jo, H.; Kim, H.; Kim, H.; Kim, S.; Kim, D. *Org. Lett.* **2005**, *7*, 75

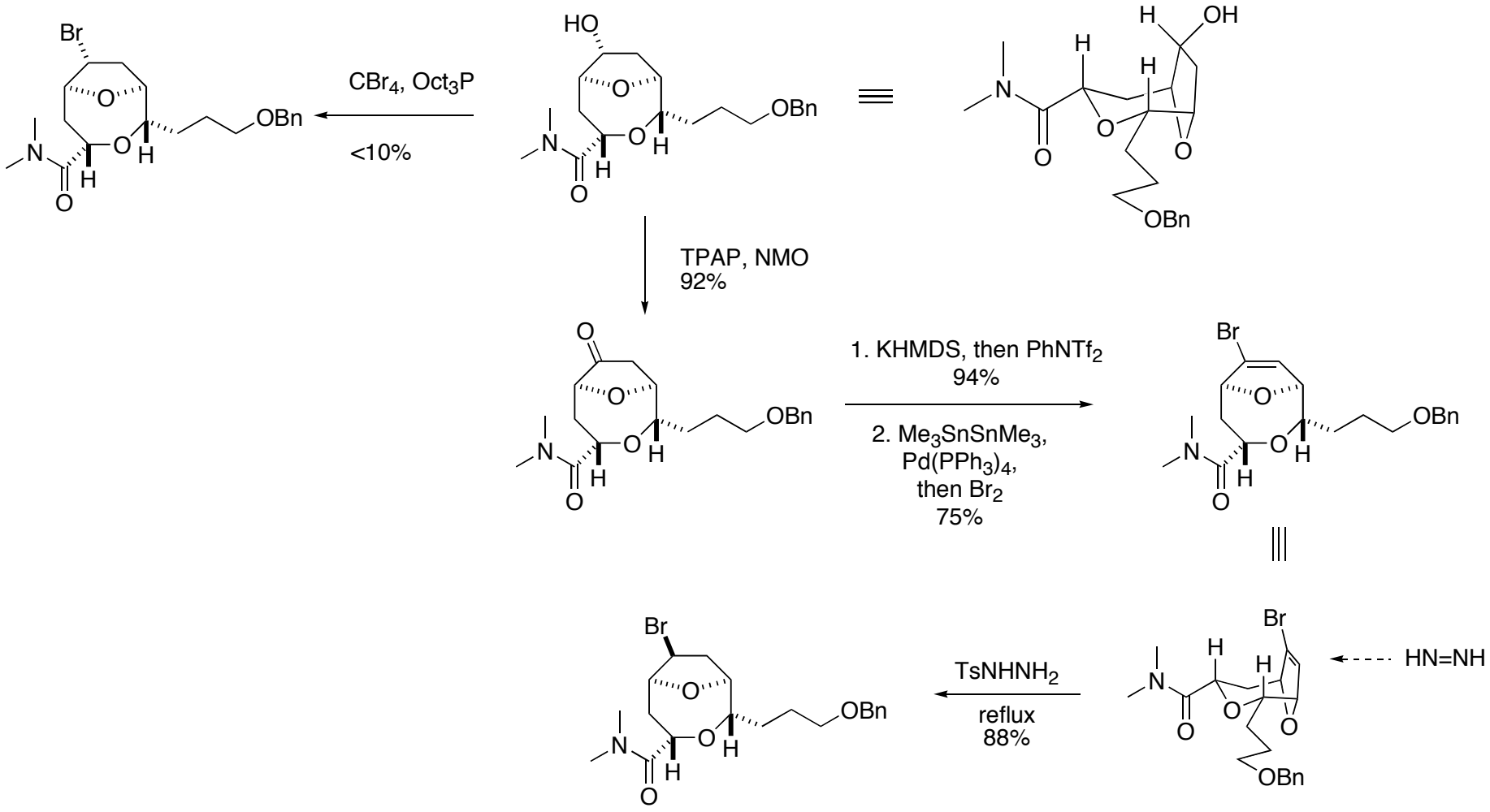
Synthesis of Common Intermediate



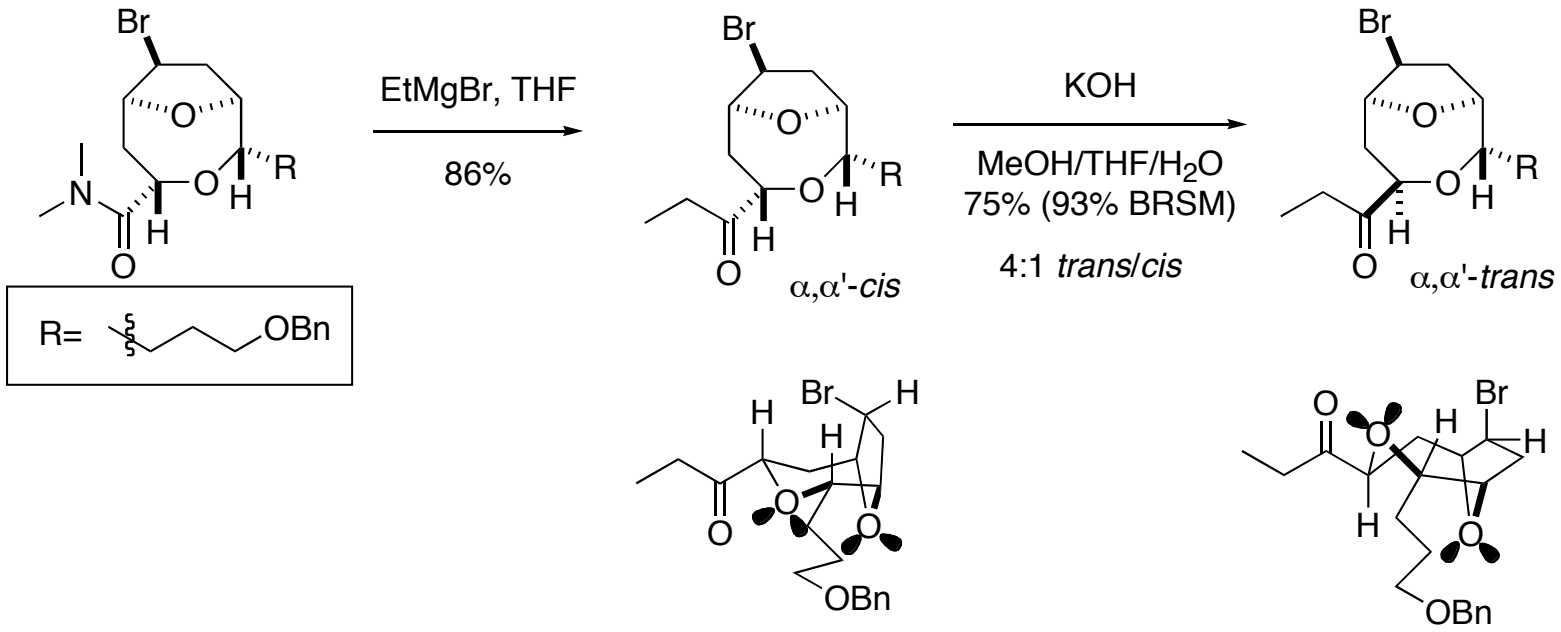
Oxetane and Oxolane formation

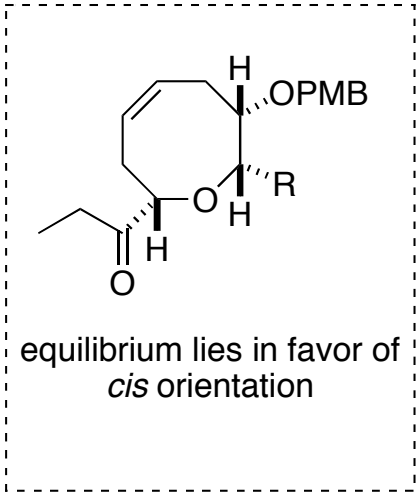


Isolaureatin Synthesis

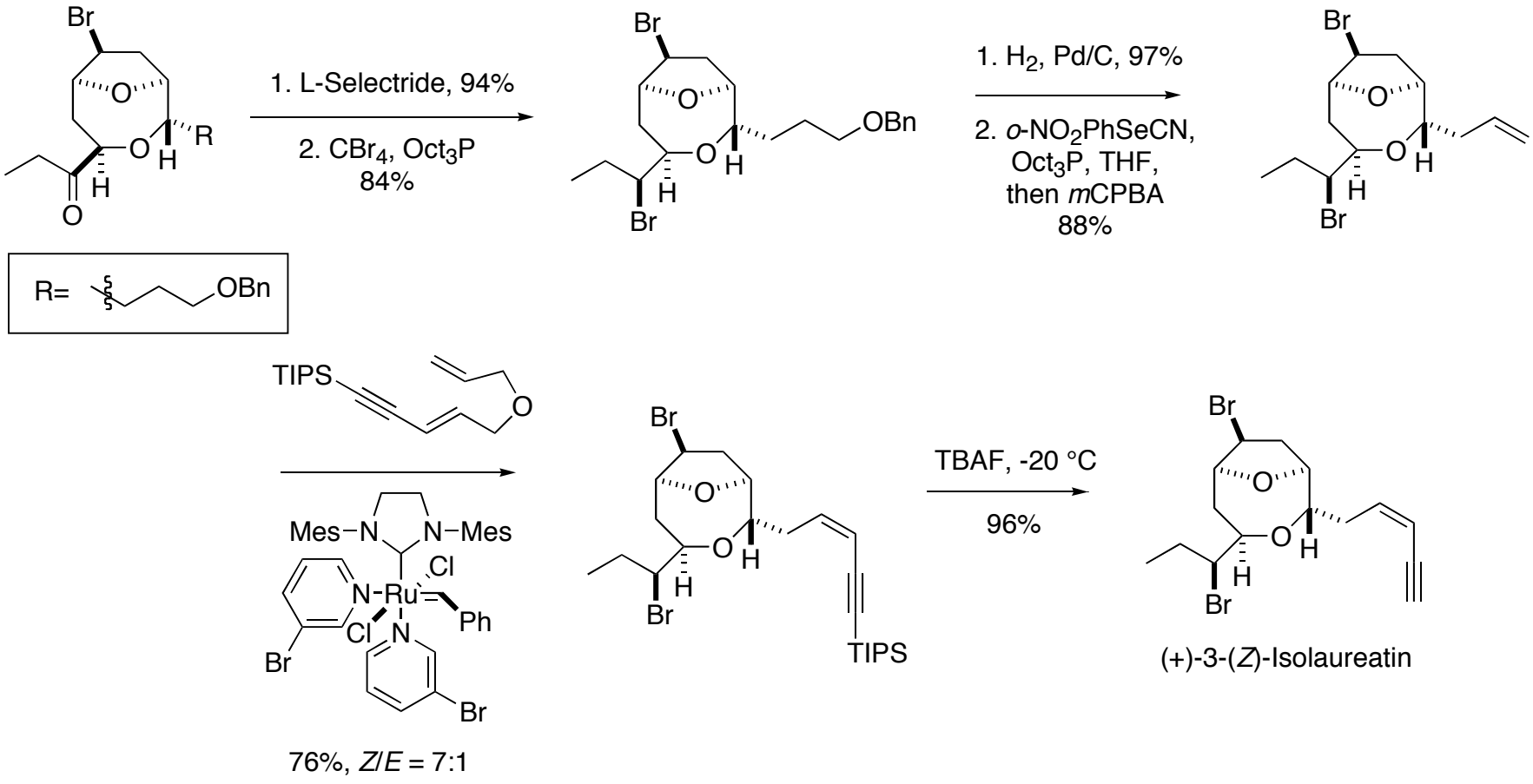


Lone Pair-Lone Pair Controlled Isomerization

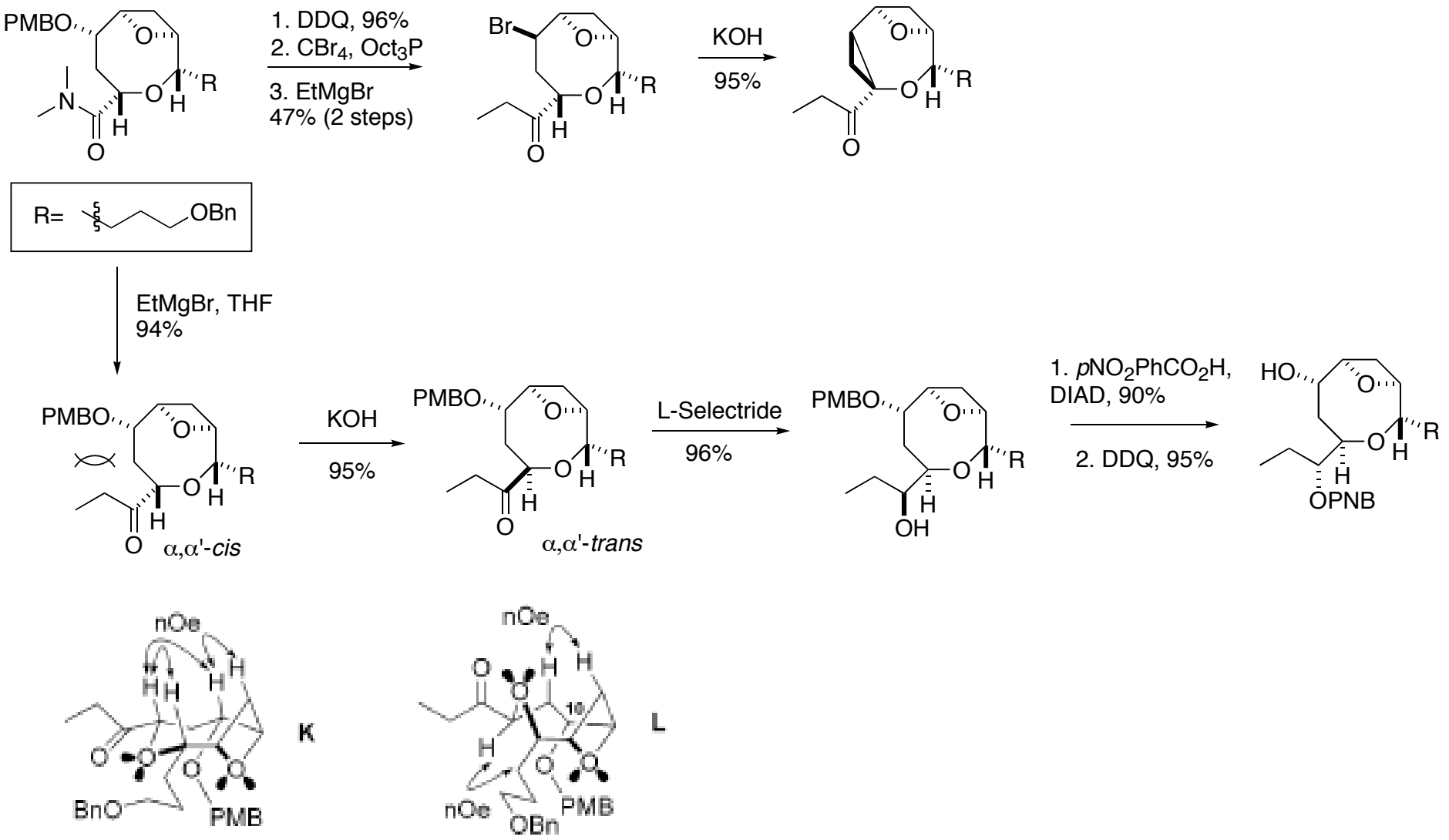




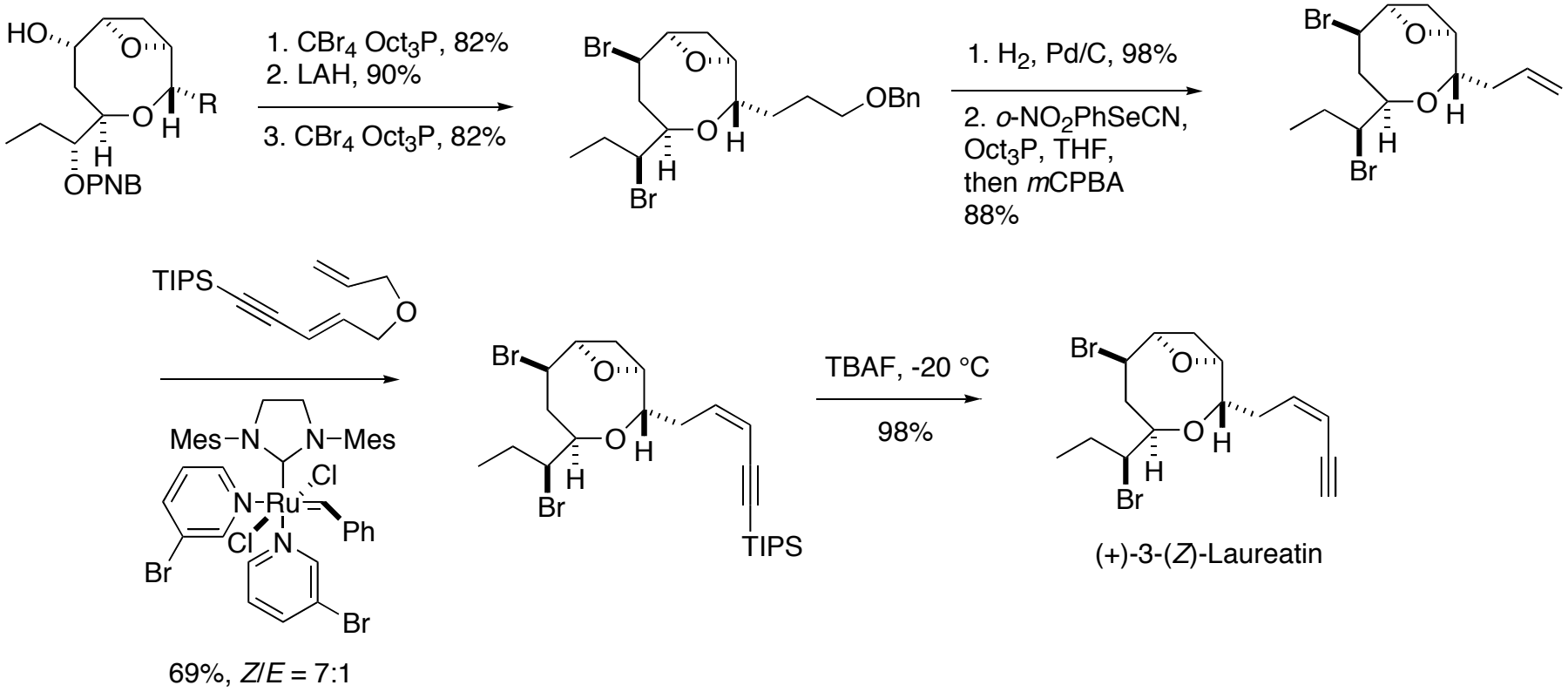
Isolaureatin Synthesis



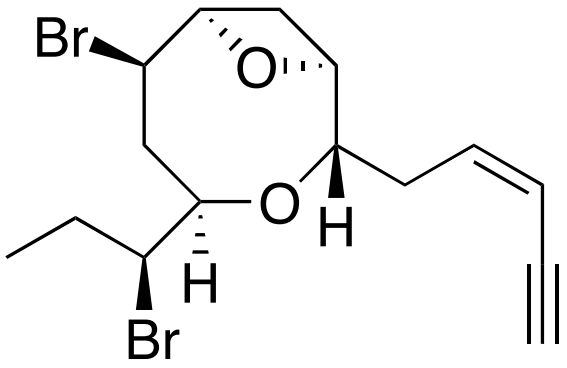
Laureatin Synthesis



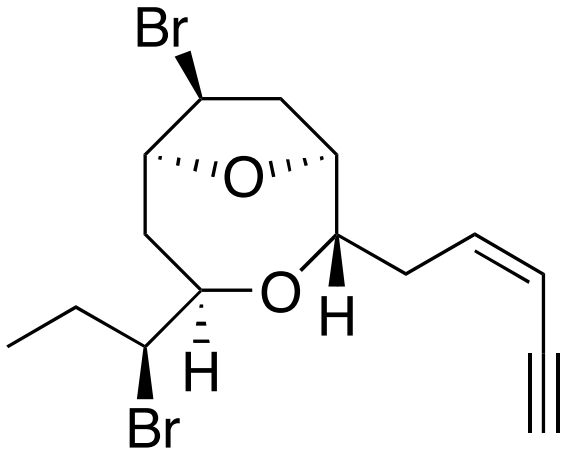
Laureatin Synthesis



Summary



(+)-3-(*Z*)-Laureatin



(+)-3-(*Z*)-Isolaureatin

- First highly stereo-, regio-, and chemoselective syntheses of the novel dioxabicyclic ring systems
- Key Steps: bromination protocols, dihydroxylation differentiation, cross metathesis, and epimerization steps
- Lone pair-controlled epimerization argument lacks support