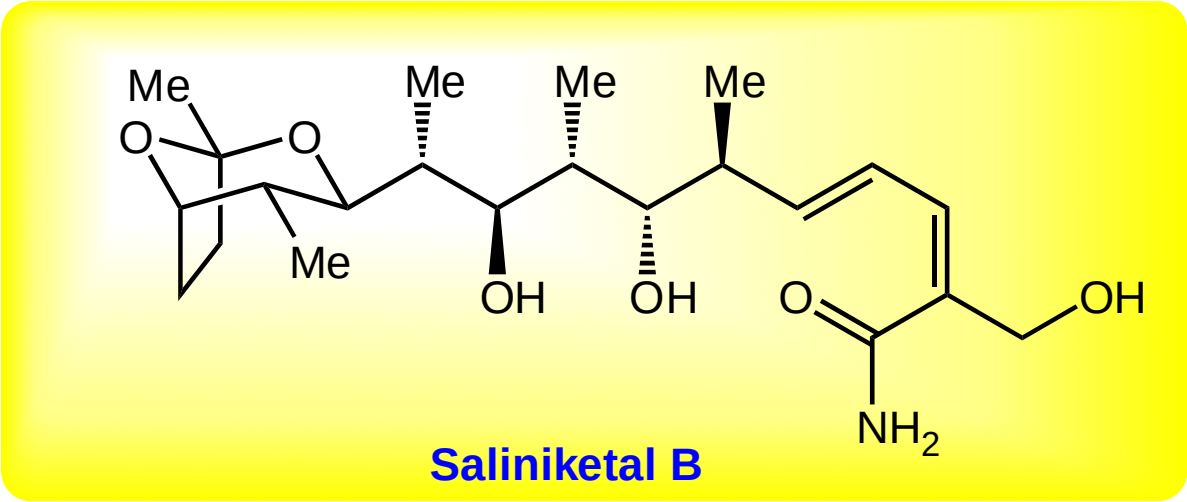
Literature Report 2009-12-22

陈庆安　　检查: 王躲生

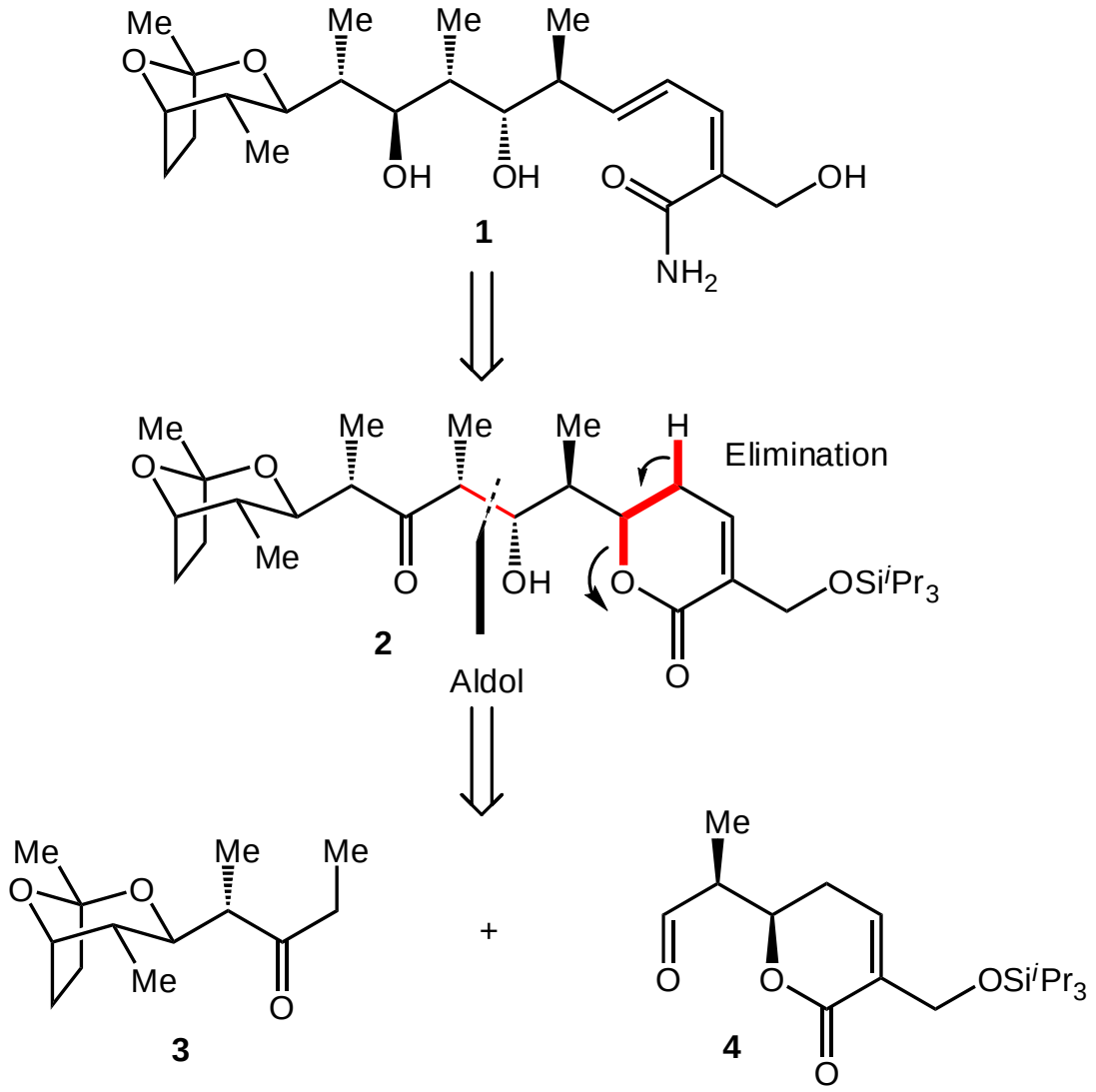
A Concise Total Synthesis of Saliniketal B

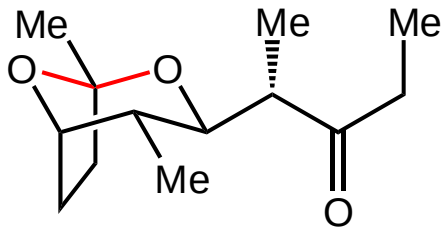
De Brabander, J. K.***** *et al*
J. Am. Chem. Soc. **2009**, *131*, 12562-12563.

Saliniketal B



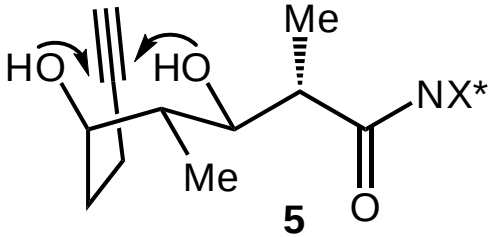
Retrosynthetic analysis of Saliniketal B



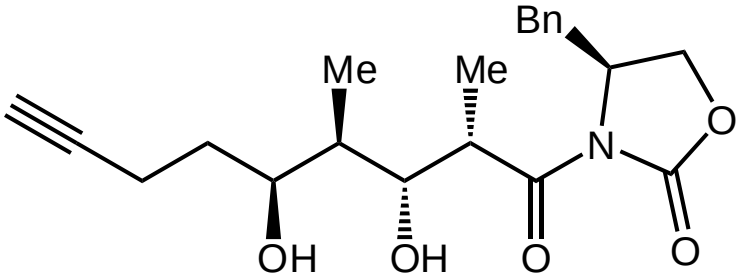


3

Cycloisomerization

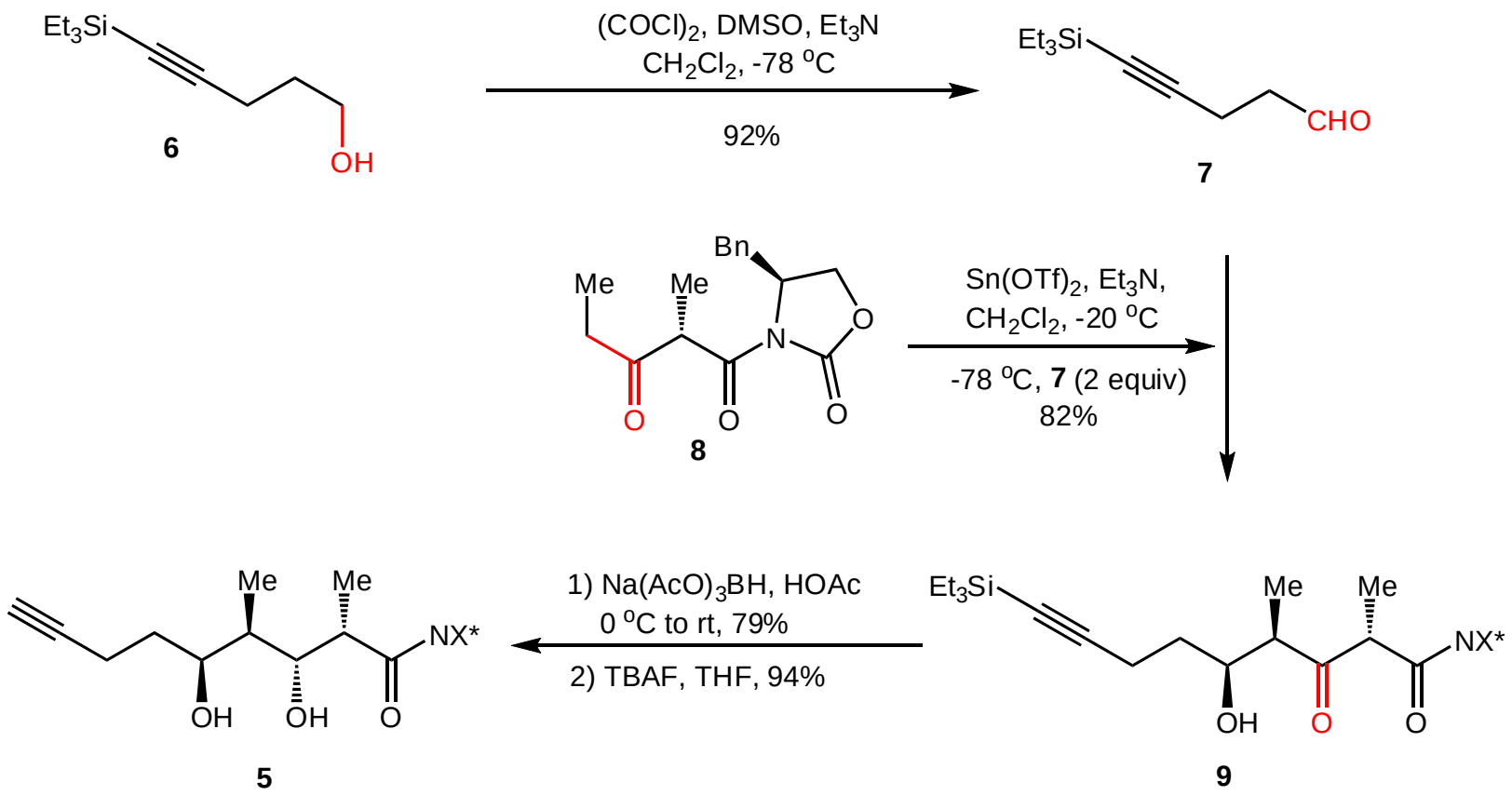


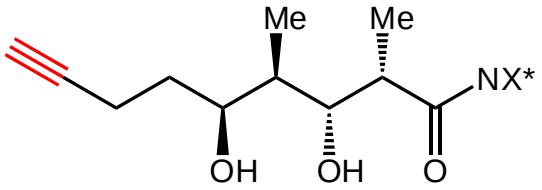
5



5

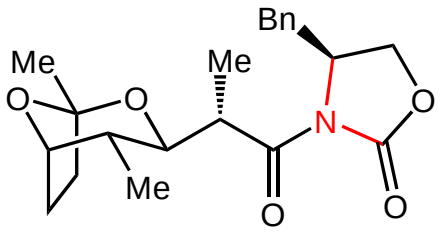
Synthesis of Fragments 3





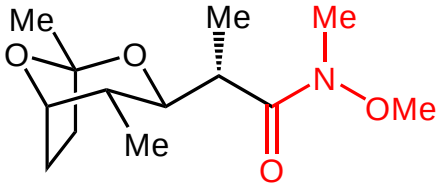
5: dr > 20/1

$[PtCl_2(CH_2CH_2)]_2$ (5 mol %)
THF, 5 min, quant.

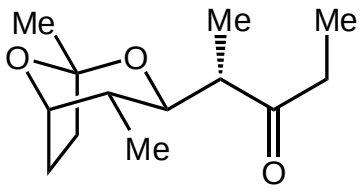


10

MeONHMe•HCl
$AlMe_3$,THF, 0 ^oC

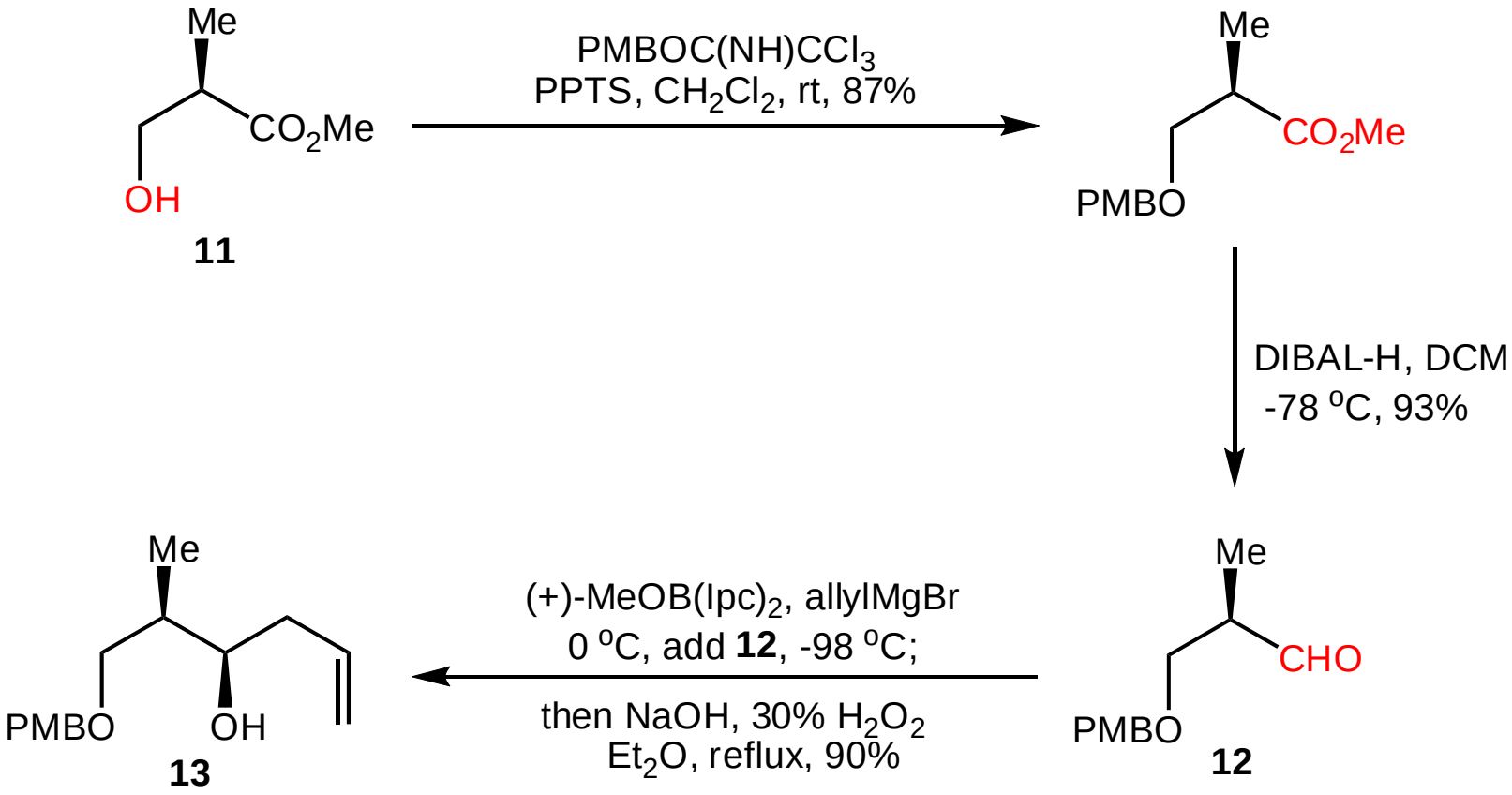


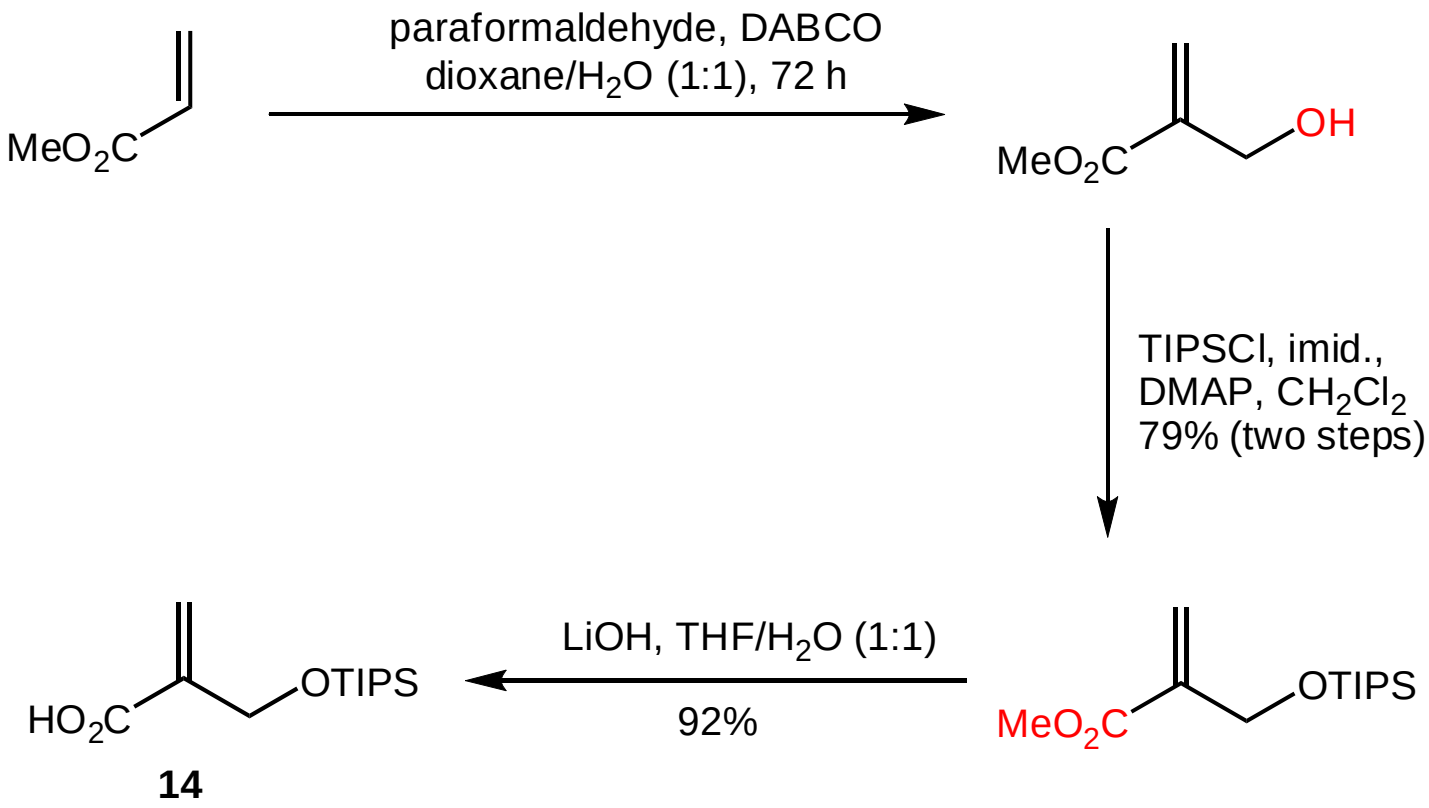
EtMgBr, THF, 0 ^oC to rt
2 h, 87% (two steps)



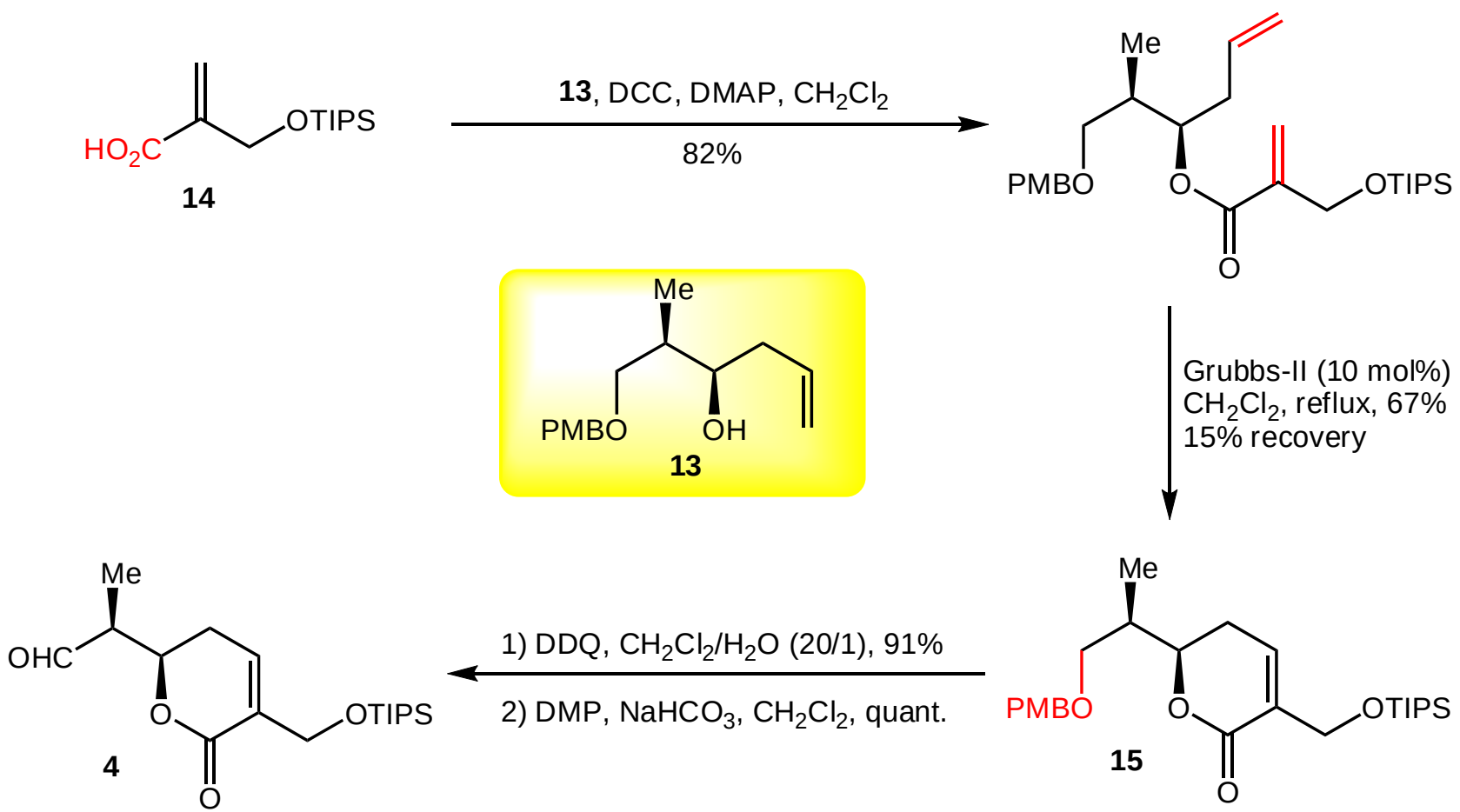
3

Synthesis of Fragments 4

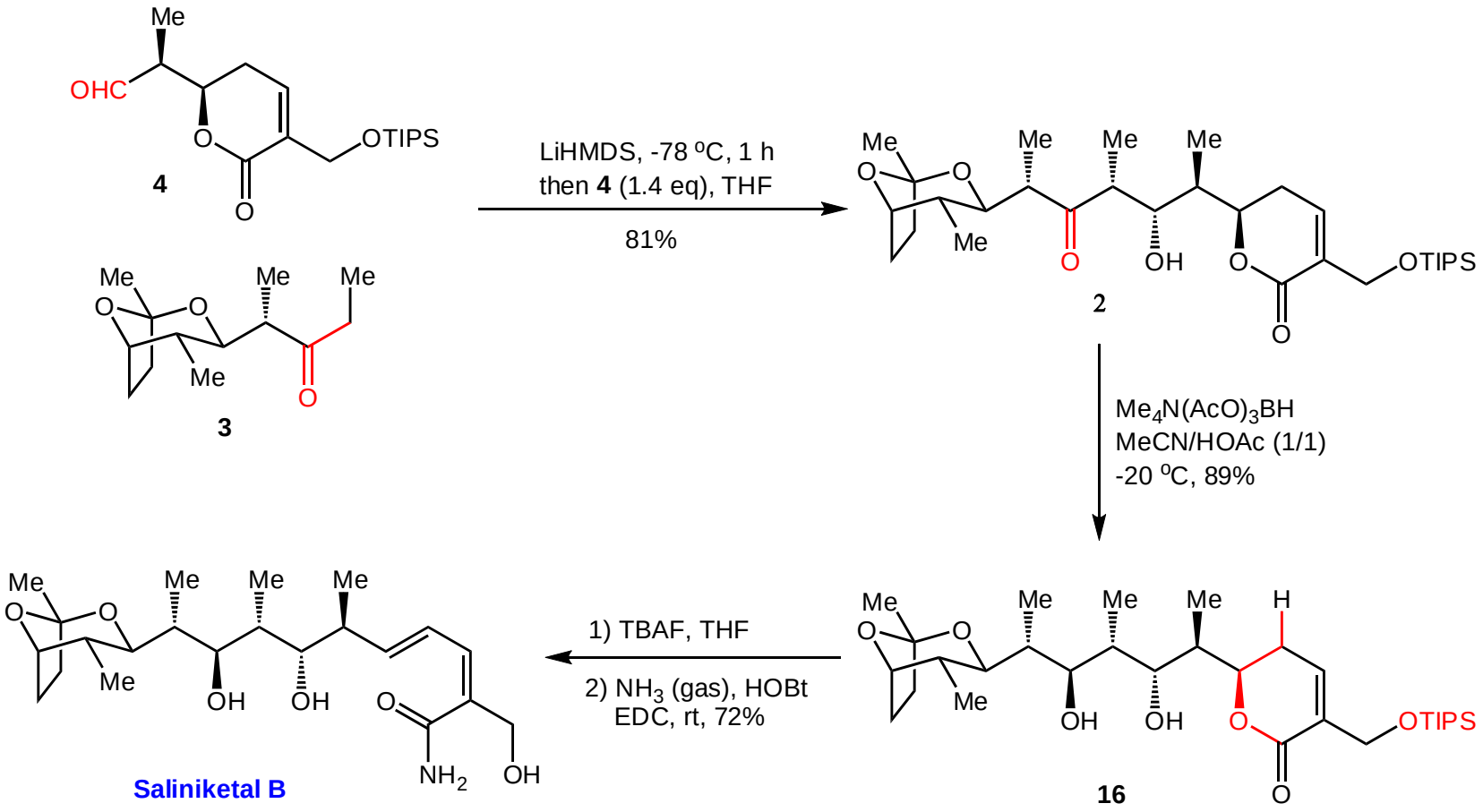



paraformaldehyde, DABCO
dioxane/H2O (1:1), 72 h
MeO2C
OH
TIPSCl, imid.,
DMAP, CH2Cl2
79% (two steps)
OTIPS
LiOH, THF/H2O (1:1)
92%
HO2C
OTIPS

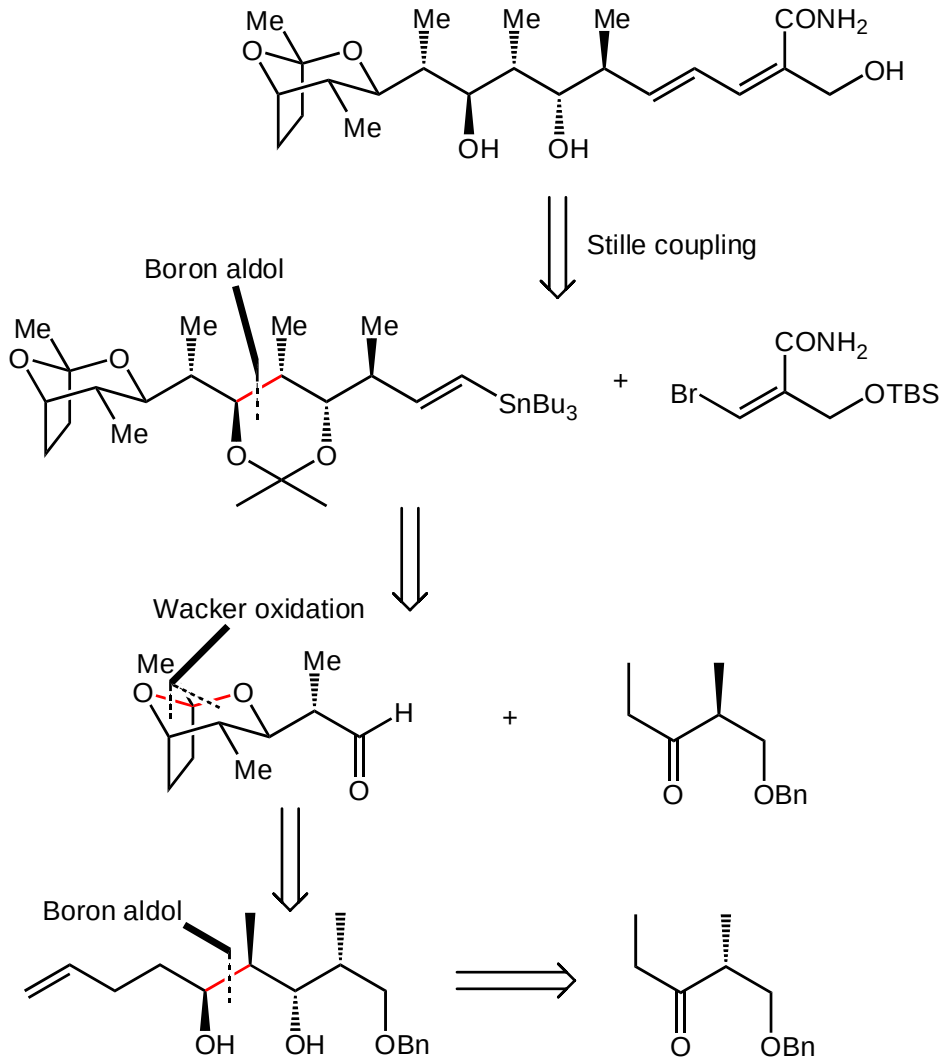
14


HO2C
OTIPS
14
13, DCC, DMAP, CH2Cl2
82%
Me
PMBO
O
OTIPS
O
Me
PMBO
OH
13
Grubbs-II (10 mol%)
CH2Cl2, reflux, 67%
15% recovery
Me
PMBO
O
OTIPS
O
15
1) DDQ, CH2Cl2/H2O (20/1), 91%
2) DMP, NaHCO3, CH2Cl2, quant.
Me
OHC
O
OTIPS
O
4

Synthesis of Saliniketal B



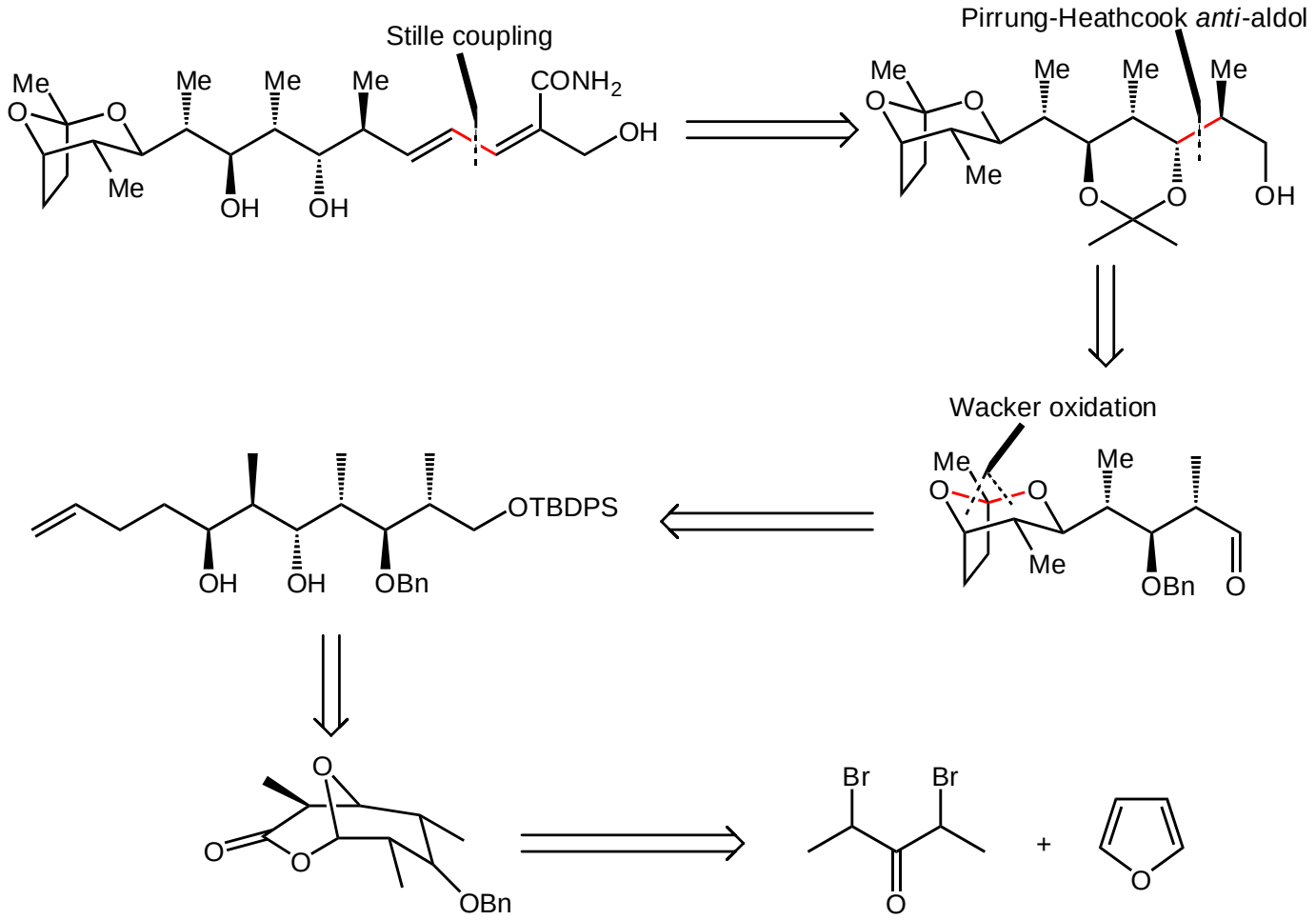
Paterson's work



17steps, 18.6%

Paterson, I. *et al*. *Org. Lett.* **2008**, *10*, 3295.

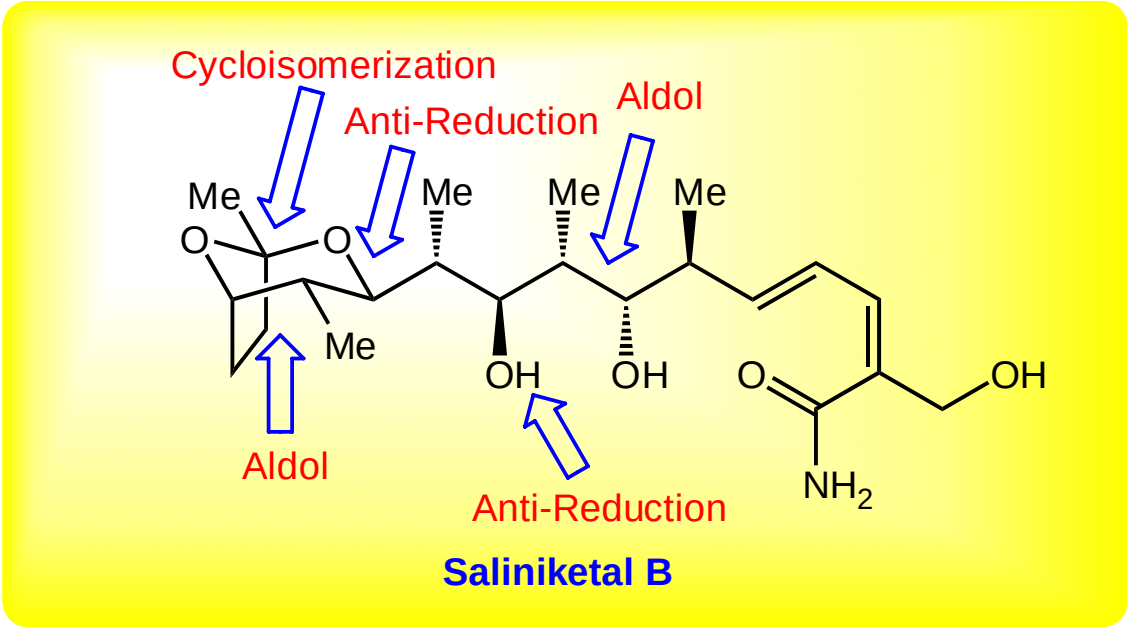
Yadav's work



19 steps, 18%

Yadav, J. S. *et al*. *J. Org. Chem.* **2009**, *74*, 8822.

Summary



11 steps, 23%

The groundbreaking work of Fenical and co-workers demonstrated that obligate marine actinomycetes are a rich source of novel bioactive natural products. In 2007, they reported the isolation of the polyketides saliniketal A and B from the marine actinomycete *Salinispora arenicola*, the structure of which was confirmed by a total synthesis of Paterson and co-workers. Besides unusual structural features, including a dioxabicyclo[3.2.1]octane ring system, an *E*,*Z*-dienamide unit, and nine stereocenters, saliniketals are of biological interest because of their ability to inhibit ornithine decarboxylase (ODC) induction. Herein, we report a concise and flexible synthesis of saliniketal B that features a strategy aimed at enabling future structure-function and mode-of-action studies.

In summary, we have achieved a short, highly efficient synthesis of saliniketal B (**1**) in 11 steps (longest linear) and 23% overall yield. Our approach features the utility of our Pt(II)-catalyzed cycloisomerization methodology for the construction of the dioxabicyclo[3.2.1]octane core, a stereoselective aldol coupling whose selectivity was positively influenced by the ketone γ-stereocenter, and an unusual one-pot desilylation/dihydropyranone fragmentation/amidation sequence.