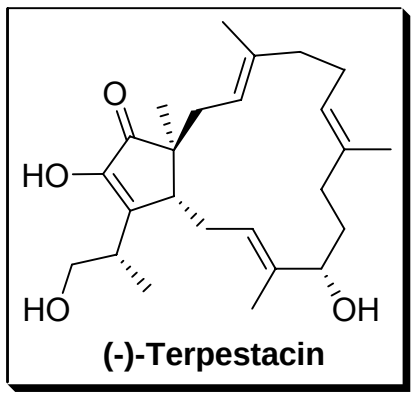
A Diosphenol-Based Strategy for the Total Synthesis of (-)-Terpestacin

Barry M. Trost, Guangbin Dong, Jennifer A. Vance
JACS, 2007, 129, 4540-4541.



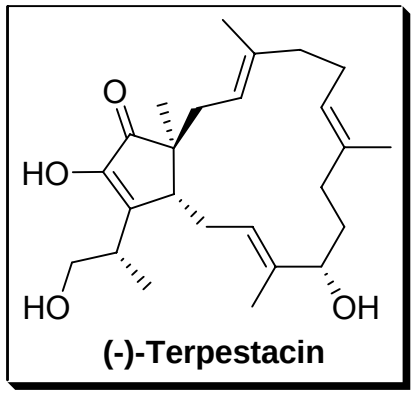
(-)-Terpestacin

Current Literature Presentation
Shuli Mao, 06/16/07

Outline

- Isolation and Biological Activities
- Previous Synthesis (3 enantioselective syn)
- Title Paper
- Summary

Isolation and Biological Activities



(-)-Terpestacin

- Originally isolated from the fungal strain *Arthrinium* sp. FA 1744 in 1993
- Found to inhibit the formation of syncytia (IC_{50} = 0.46 μg/mL) (giant-multinucleated cells that arise from the expression of gp120 on cell surfaces in the course of HIV infection)
- Found to inhibit angiogenesis

Oka, M. *et al J. Antibiot.* **1993**, *46*, 367.
Kwon, H. J. *et al J. Antibiot.* **2003**, *56*, 492.

Previous Synthesis

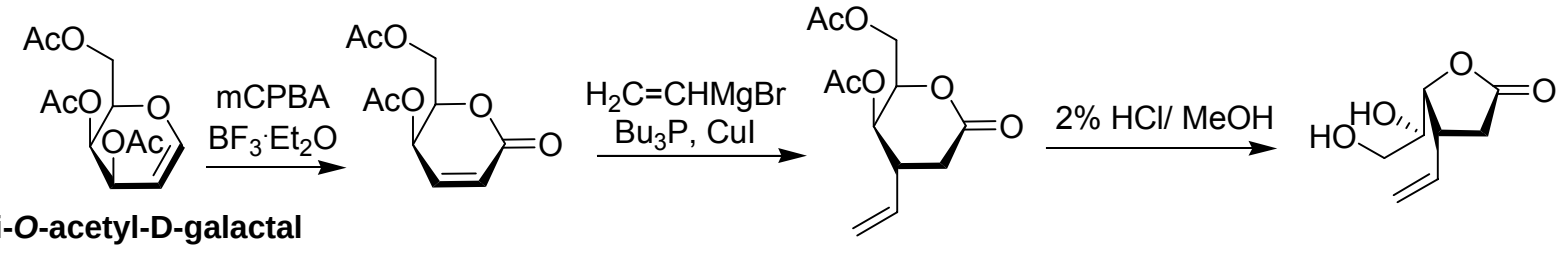
- Total Synthesis:

1. Kuniaki Tatsuta: **1998** (1st racemic and enatioselective)
2. Andrew Myers: **2002** (enatioselective)
3. Timothy Jamison: **2003** (enatioselective)

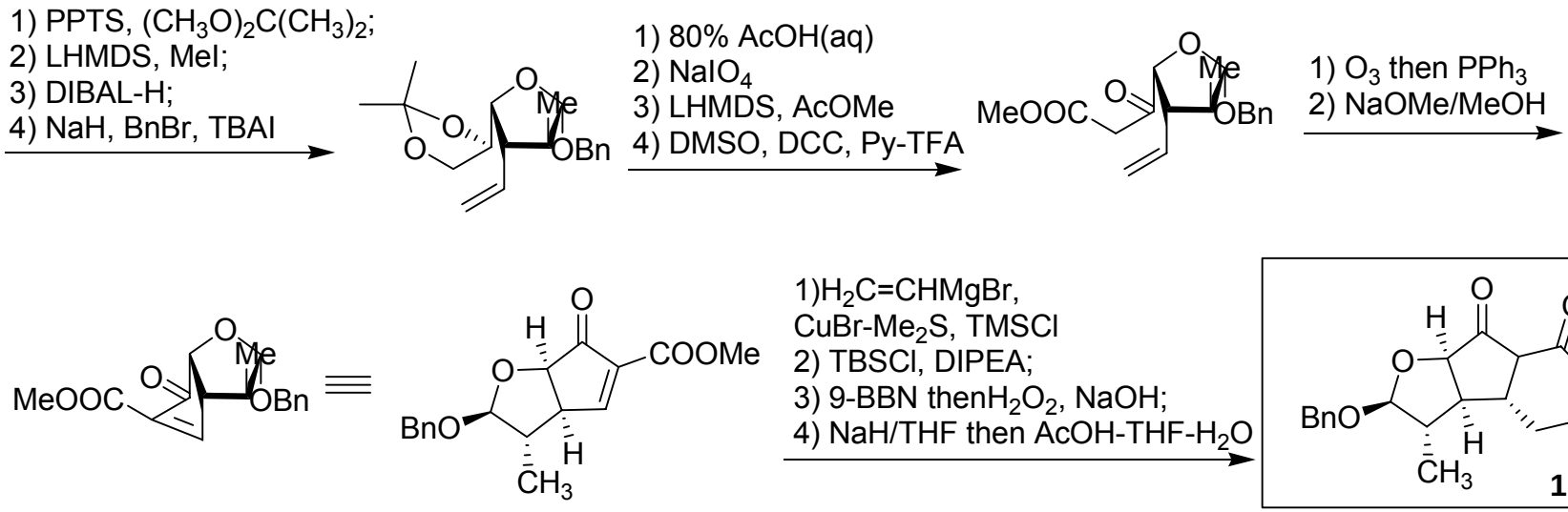
- Partial or Core Synthesis:

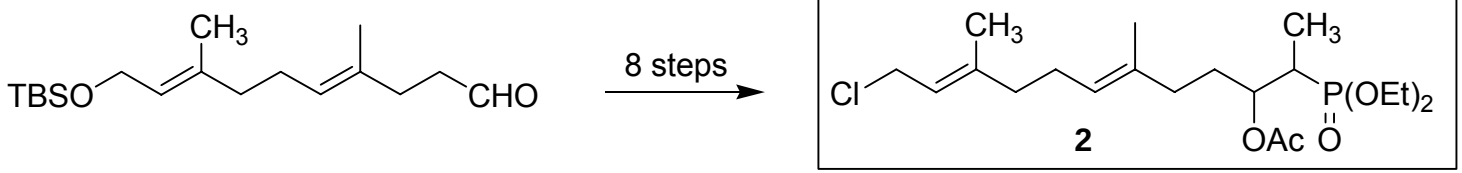
1. Kei Takeda & Eiichi Yoshii: **1995**
2. Denis Heissler: **1999**
3. Marcus Tius: **2005**

Tatsuta Synthesis



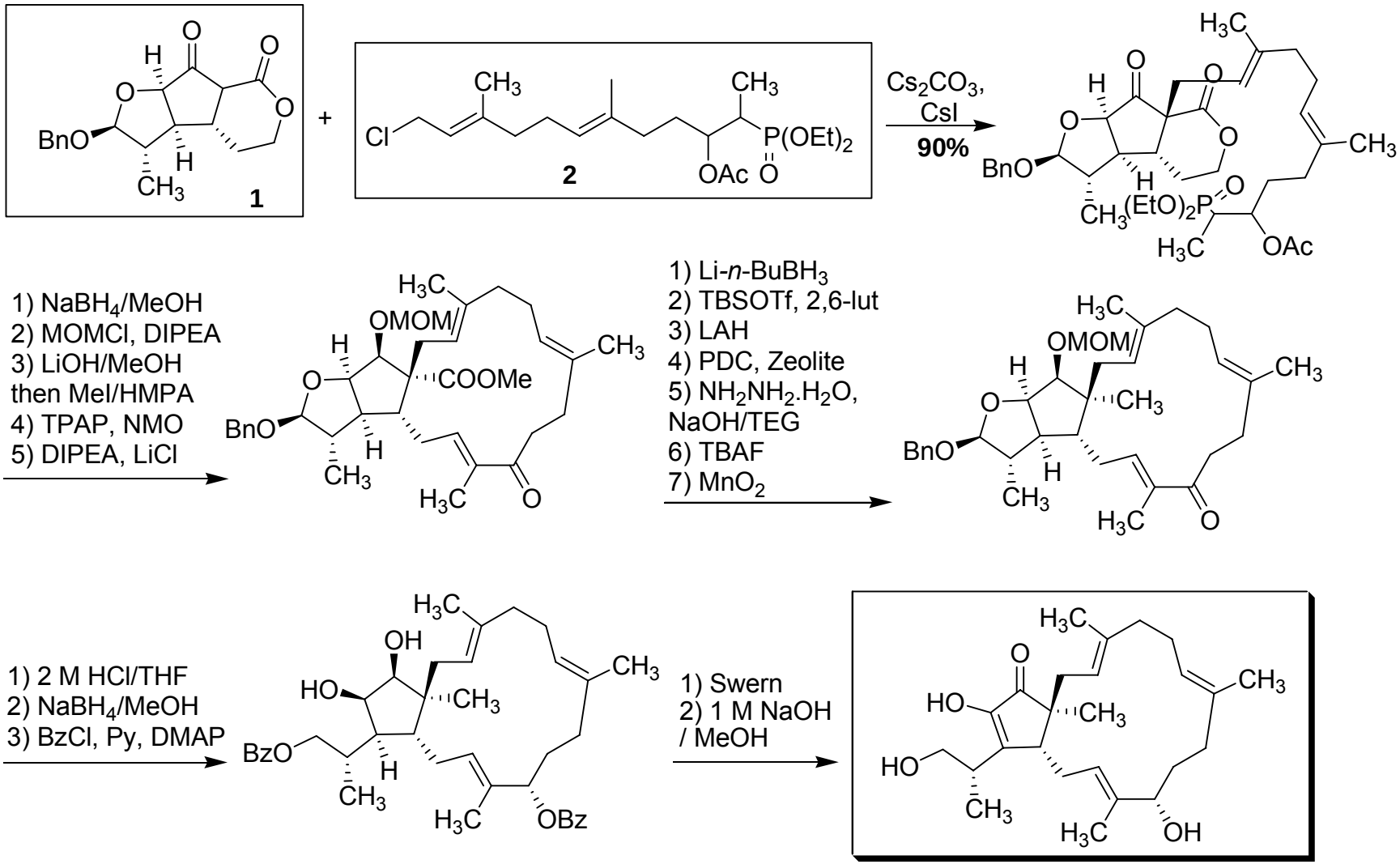
Tri-*O*-acetyl-D-galactal



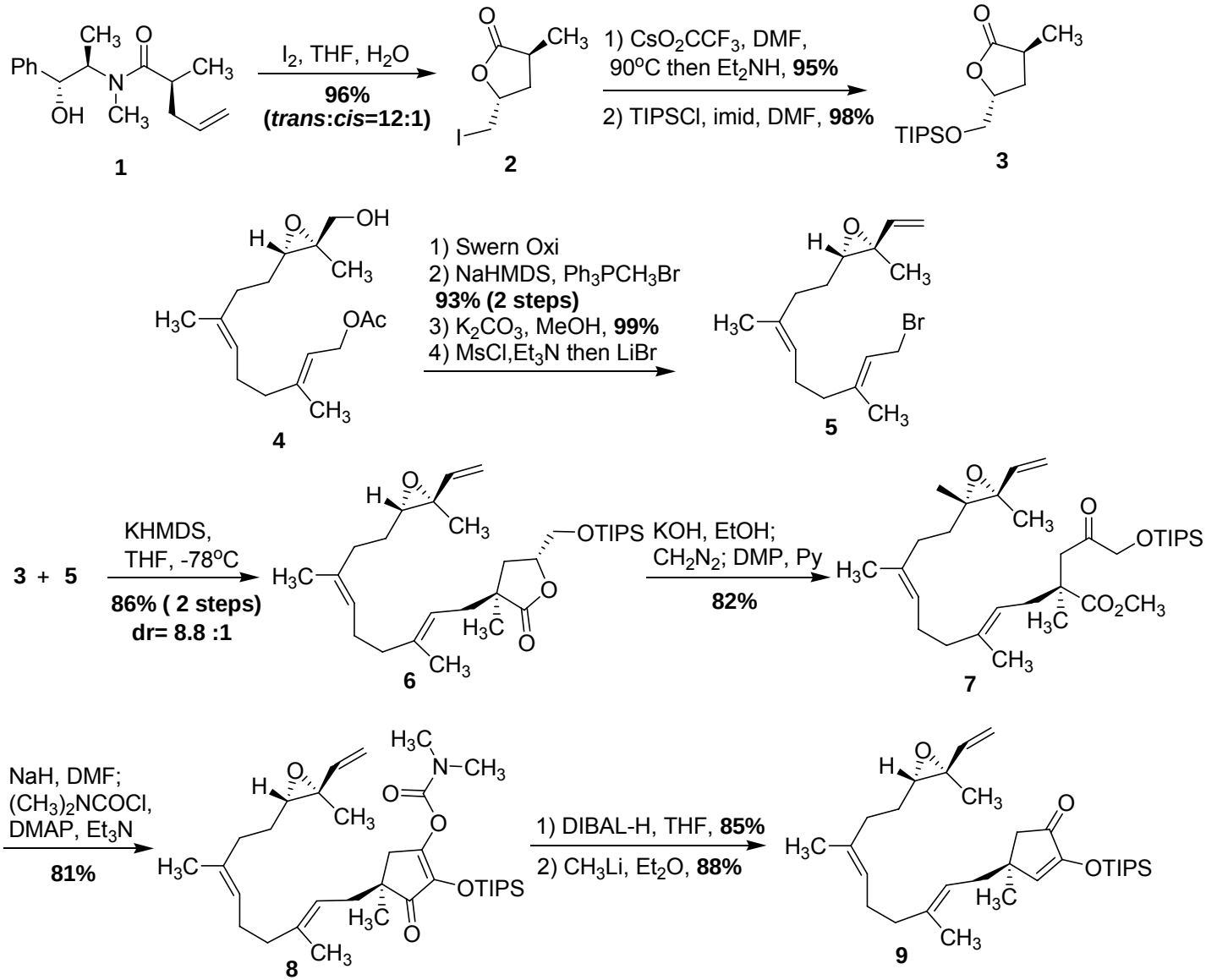


Tatsuta, K.; Masuda, N. *J. Antibiot.* **1998**, *51*, 602.

Tatsuta Synthesis (Cont'd)

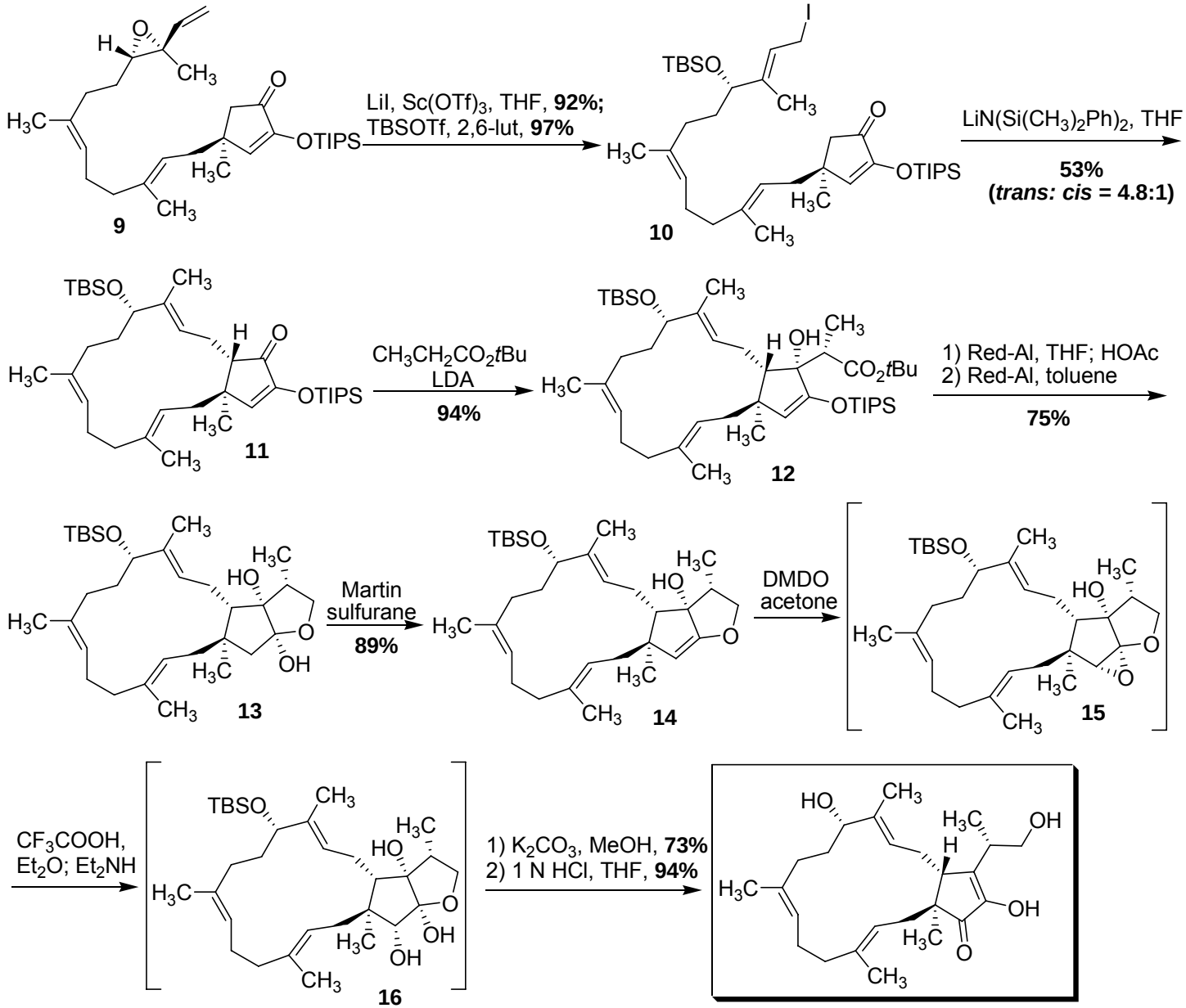


Myers Synthesis

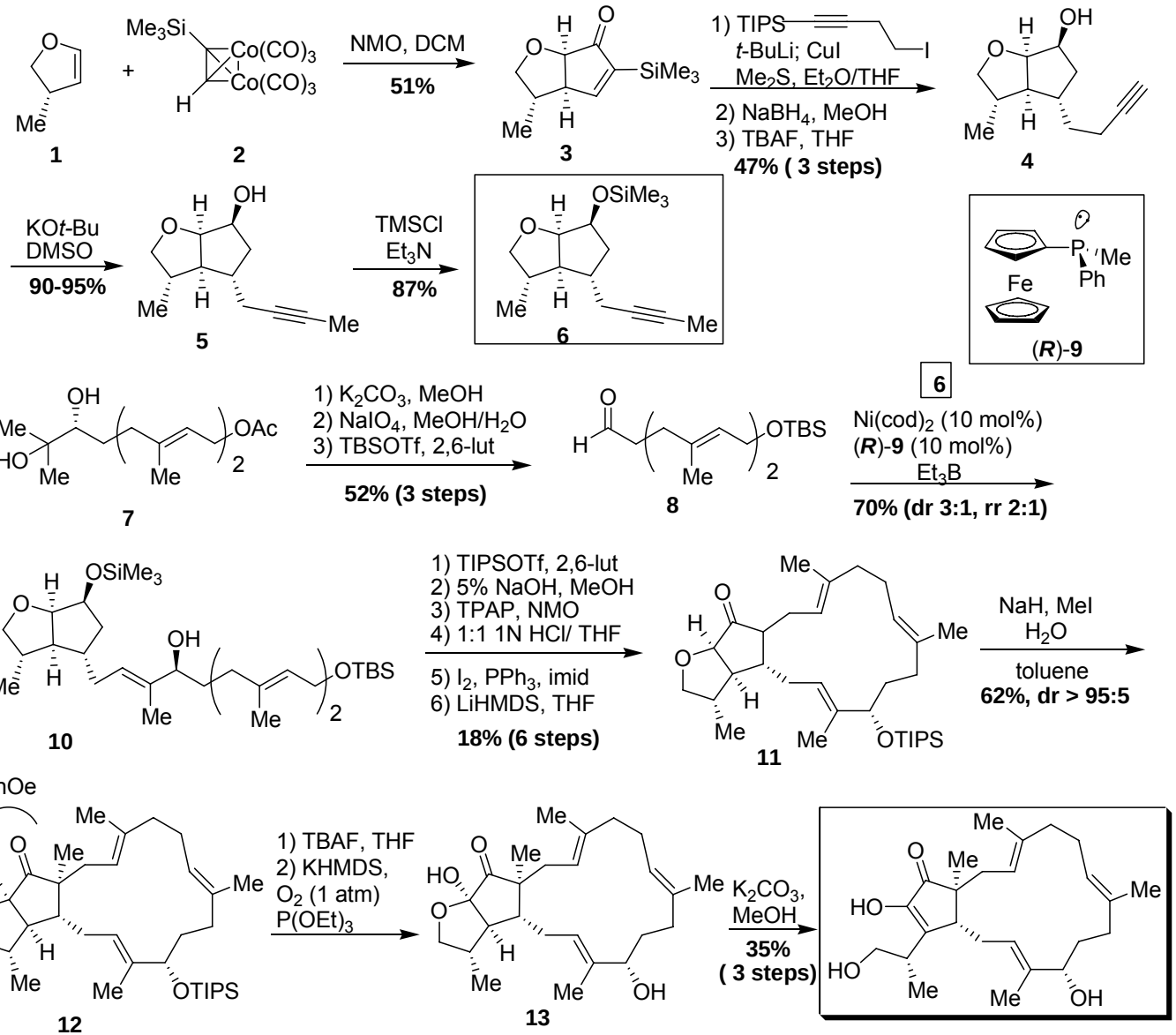


Myers, A. G.; Siu, M. *J. Am. Chem. Soc.* **2002**, *124*, 4230.

Myers Synthesis (Cont'd)

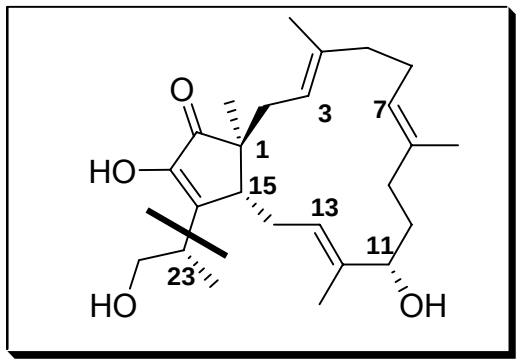


Jamison Synthesis



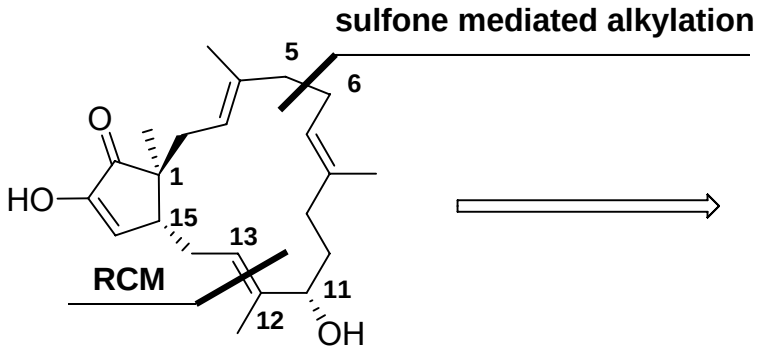
Chan, J.; Jamison, T. F. *J. Am. Chem. Soc.* **2003**, *125*, 11514.

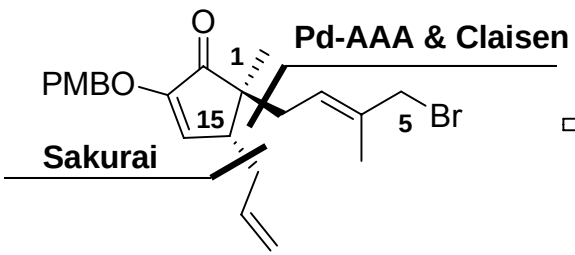
Title Paper:Trost Retrosynthesis



Pd-AAA & Claisen

sulfone mediated alkylation





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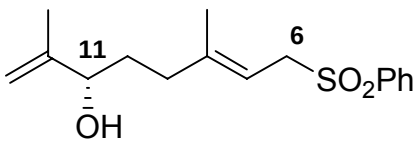
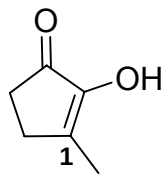
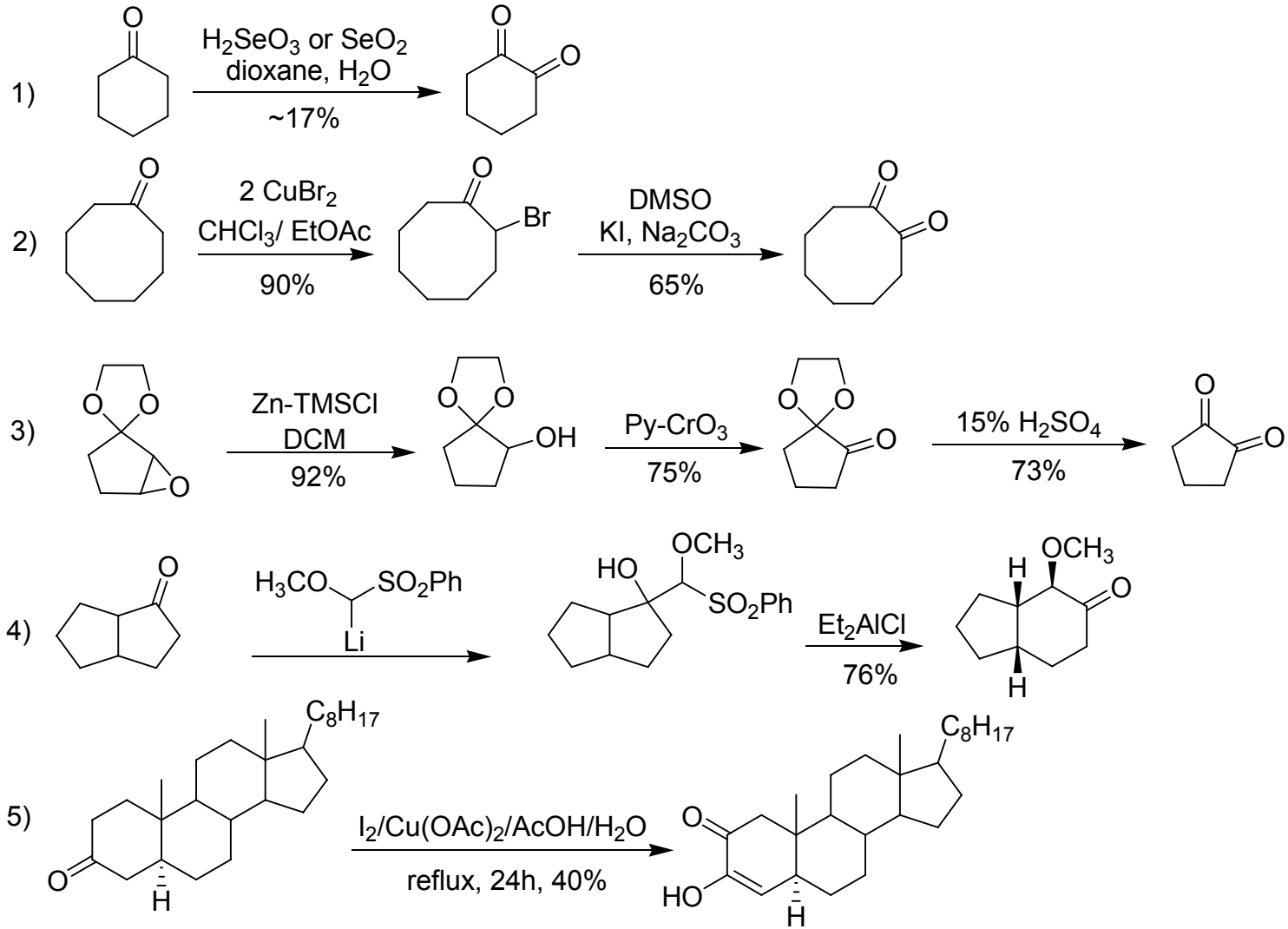




3-methyl-1,2-cyclopentanedione

Trost, B. M.; Dong, G.; Vance, J. A. *J. Am. Chem. Soc.* **2007**, *129*, 4540.

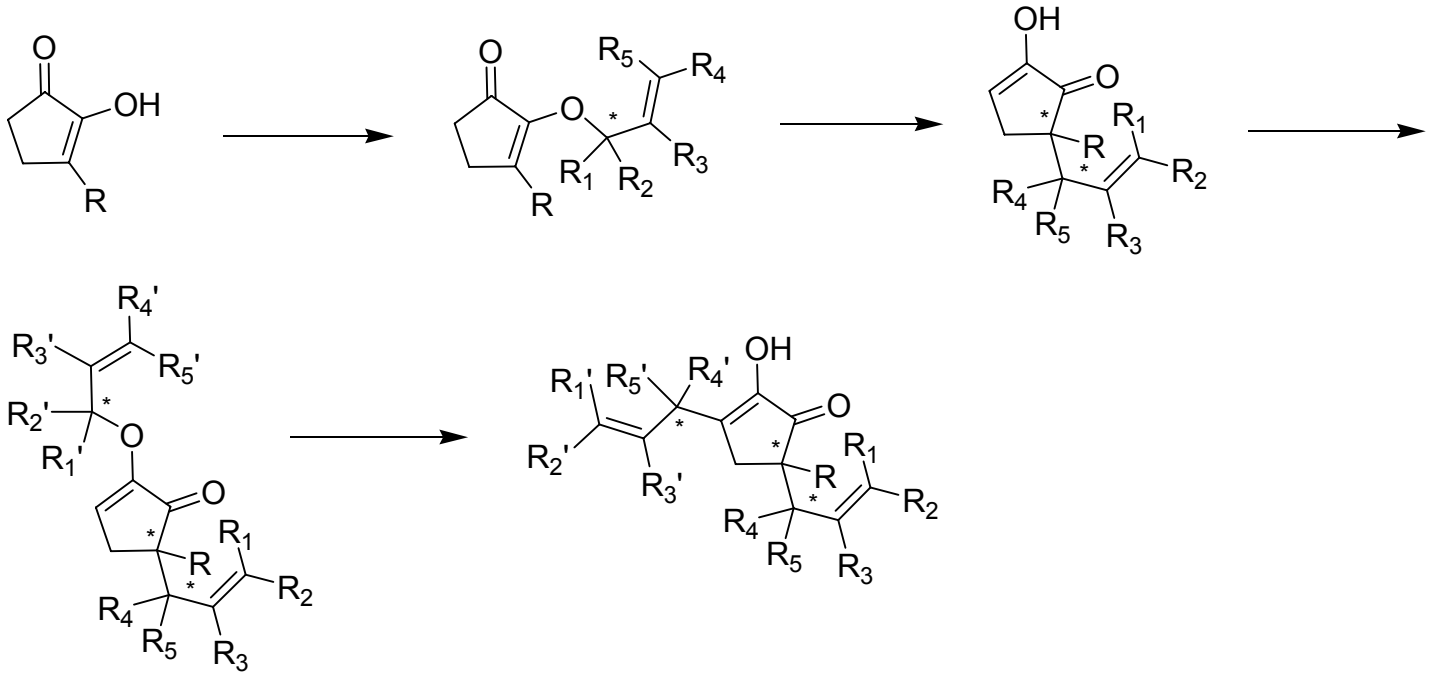
Synthesis of Cyclic 1,2-Diketones



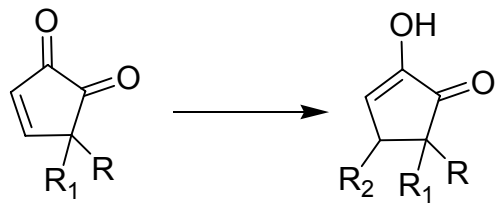
1) Hach, *et. al*, *Org. Syn.***1963**, 229. 2) Macomber, *et. al*, *J. Org. Chem.* **1975**, *40*, 1990. 3) Vankar, *et. al*, *Tetrahedron Lett.* **1987**, *28*, 551. (4) Trost, *et. al*. *J. Am. Chem. Soc.* **1987**, *109*, 4124. (5) Horiuchi, *et. al*. *Synthesis* **1989**, *10*, 785.

Title Paper: Diosphenol-Based Strategy

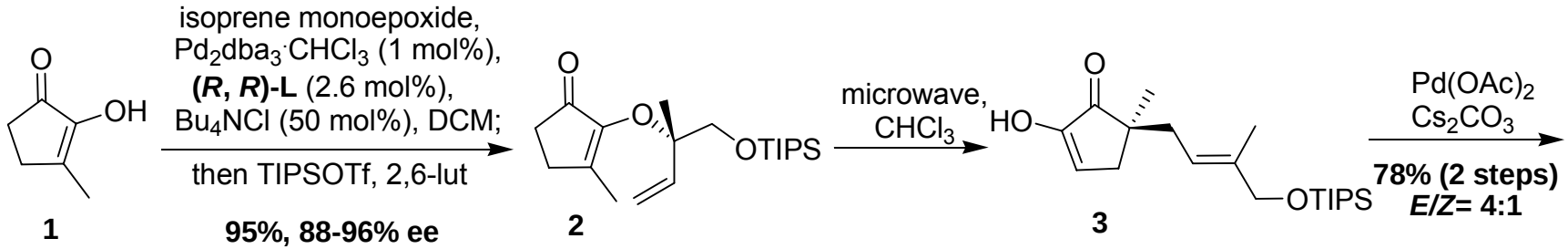
Strategy 1: Pd-AAA & Claisen rearrangement

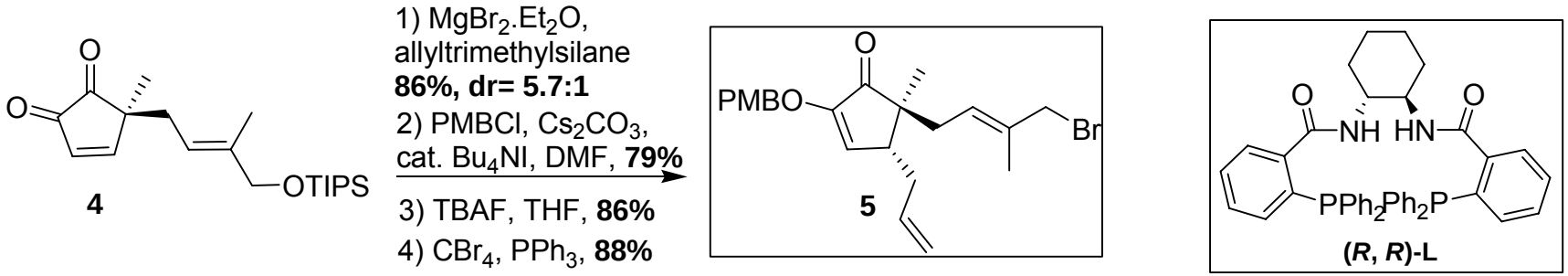


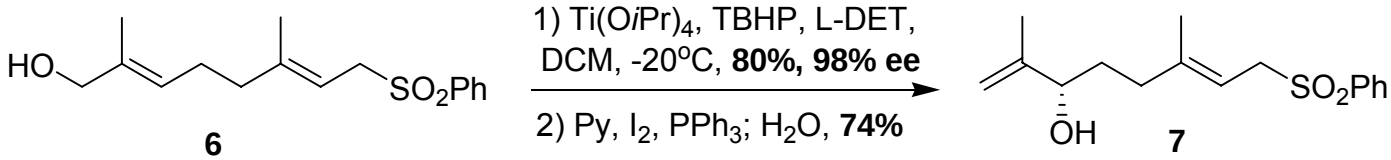
Strategy 2: Michael addition

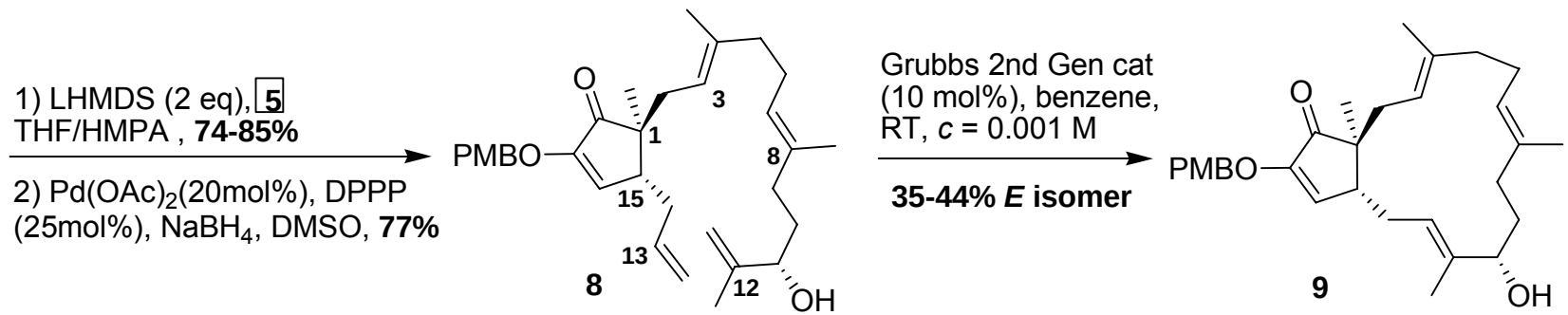


Title Paper:Trost Synthesis

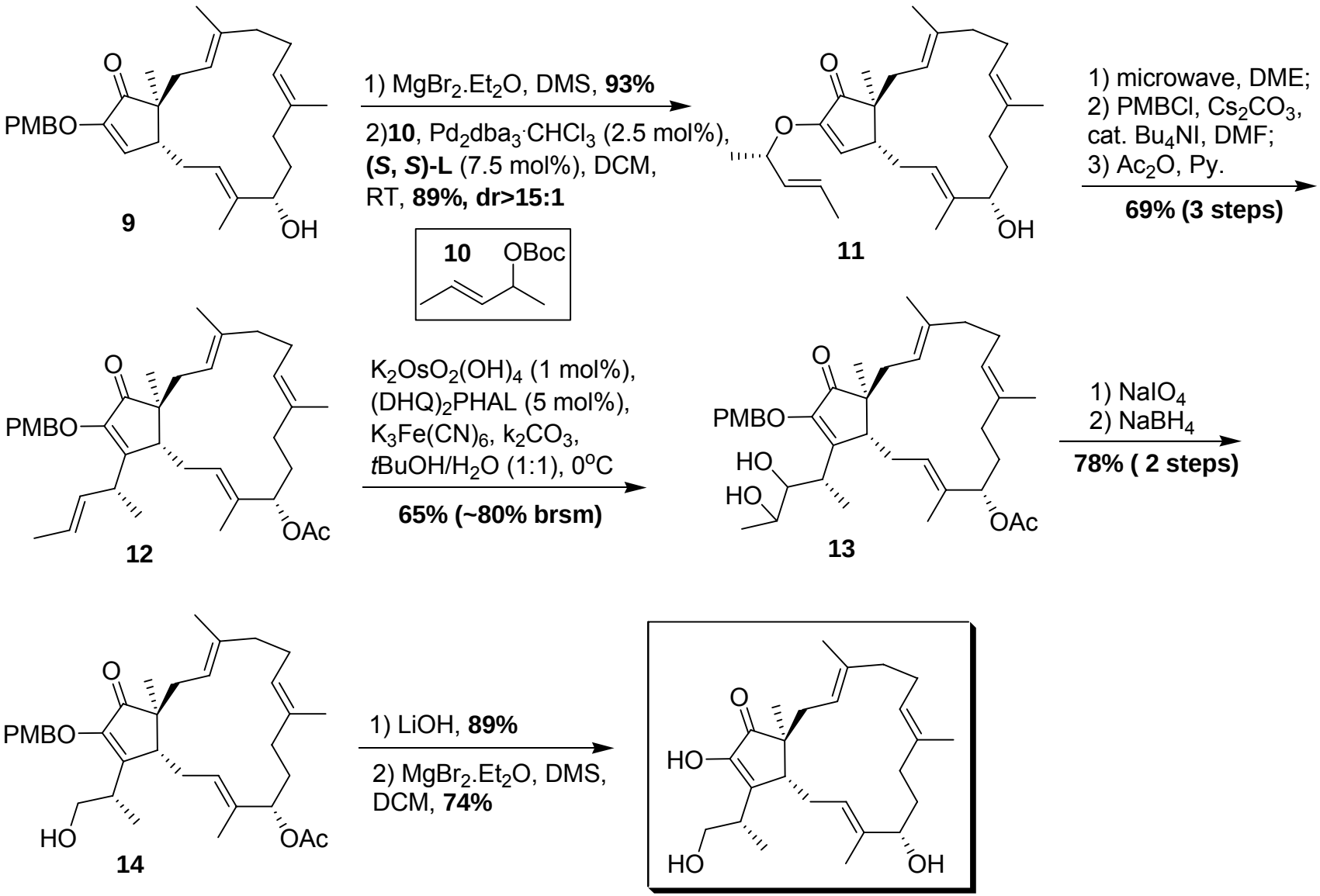








Title Paper:Trost Synthesis (Cont'd)



Summary

	Steps	Yields	Key Transformations
Tatsuta	38 (from tri-*O*-acetyl-D-galactal)	0.45%	alkylation & HWE
Myers	20 (from $ (*R,R*)-pseudoephedrine propionamide)	5.4%	alkylation
Jamison	20 (from $ β-methallyl alcohol)	0.06%	alkylation & reductive coupling between aldehyde and alkyne
Trost	19 (from $ 3-methyl-1,2-cyclopentanedione)	0.2%	sulfone mediated alkylation, RCM, Pd-AAA & Claisen