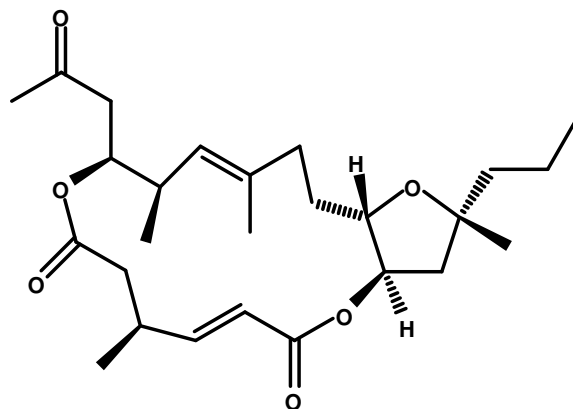


Amphidinolide X



Molecule in Review

Steven Breazzano (Snyder Group)

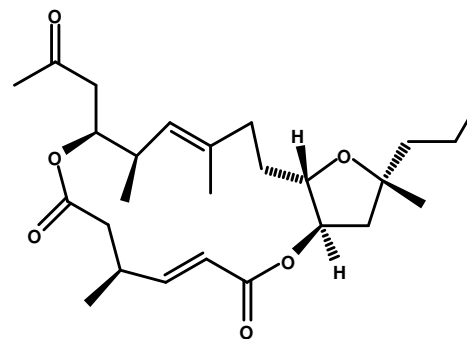
Synthesis Literacy Group

7/31/09

Columbia University Chemistry

Introduction

- Derived from marine dinoflagellates of the genus *Amphidinium*, living in symbiosis with the Okinawan flatworm *Amphiscolops*.
- Absolute and relative configurations determined by long range NMR and degradation studies
- First macrodiolide consisting of polyketide-derived diacid and diol units from natural sources
- Biosynthetic origins investigated by means of feeding experiments with ^{13}C -acetates
- Moderate cytotoxicity against L1210 and KB cell lines



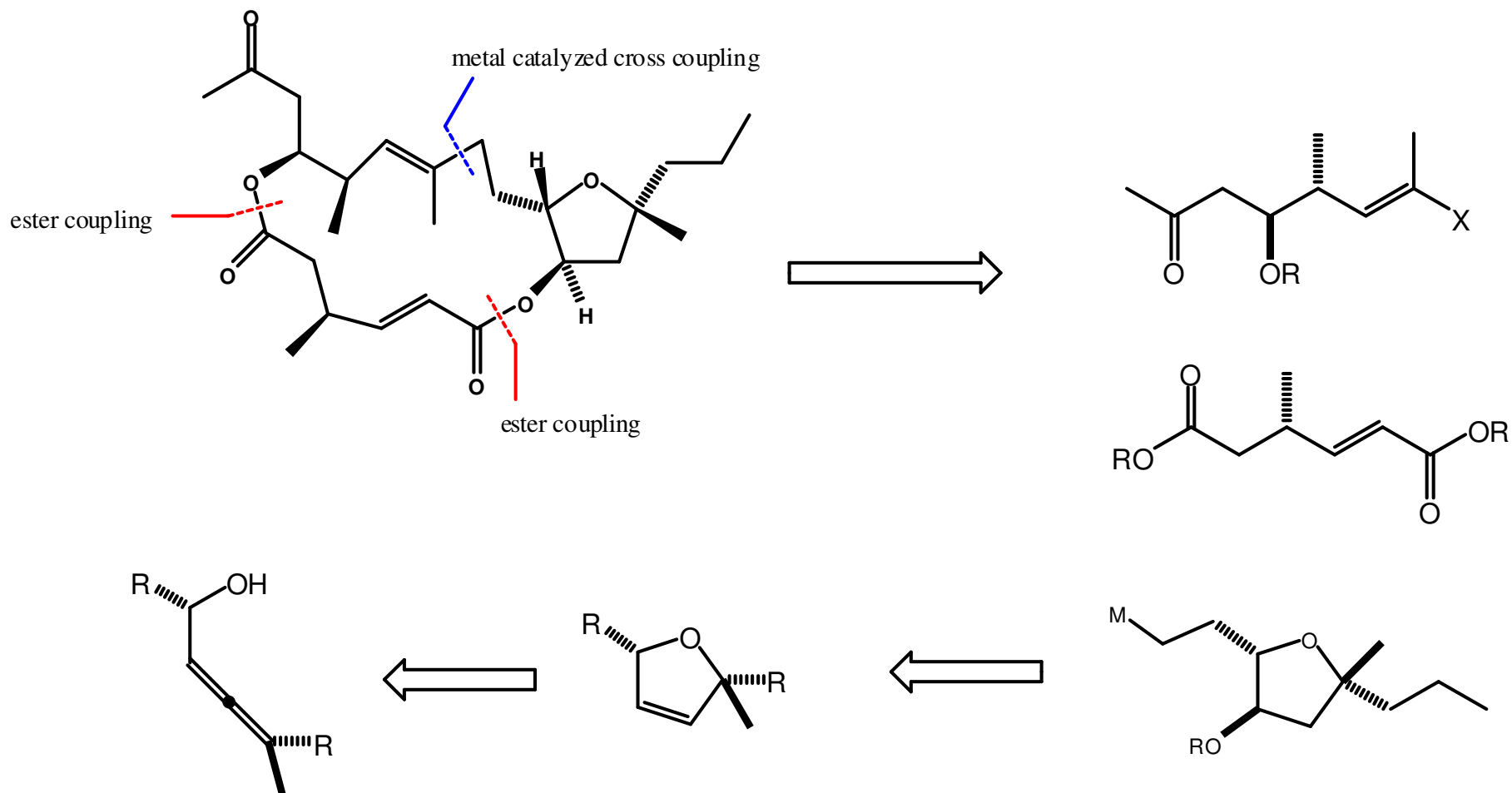
Isolation: Kobayashi, et al. JOC. 2003, 68, 5339

Breazzano 2 - CU Synthesis Lit Group – Amphidinolide X

Introduction

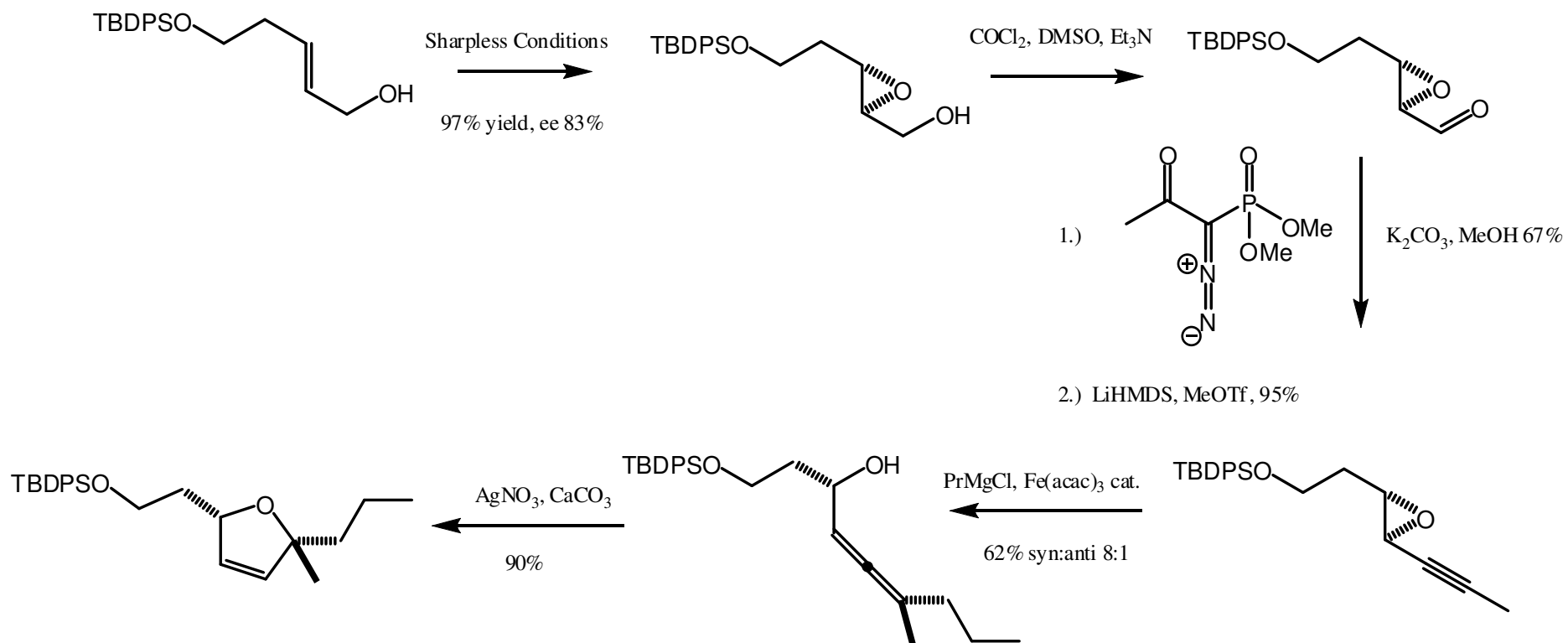
- Syntheses and methods examined
 - Furstner (2004) First total synthesis
 - Olivier Lepage, Egmont Kattnig, Alois Furstner. *JACS*, **2004**, *126*, 15970
 - Wei-Min Dai (2006) Synthesis of THF moiety (formal synthesis)
 - Dai, et al. *Synthesis*, **2006**, *8*, 1177
 - Vilarrasa (2008) Total synthesis *via* RCM
 - Vilarrasa, et al. *Org. Lett.*, **2008**, *10*, 5191
 - Lee (2009) New method for tetrahydrofuran synthesis
 - Jae Hoon Jung, Eun Lee. *ACIEE*, **2009**, *48*, 5698

Furstner Synthesis - Retrosynthesis



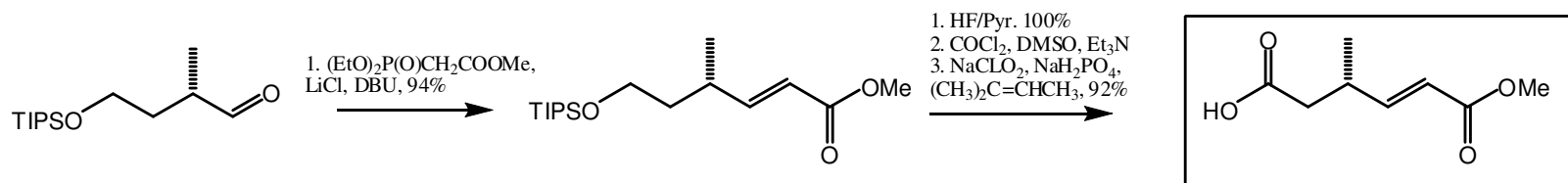
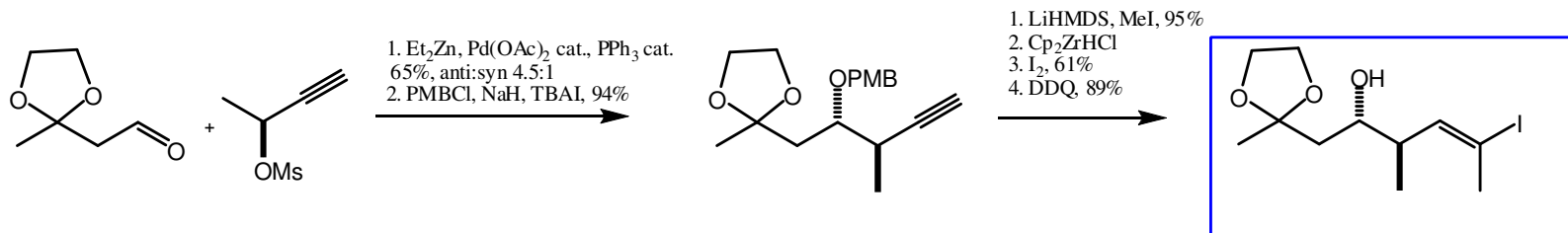
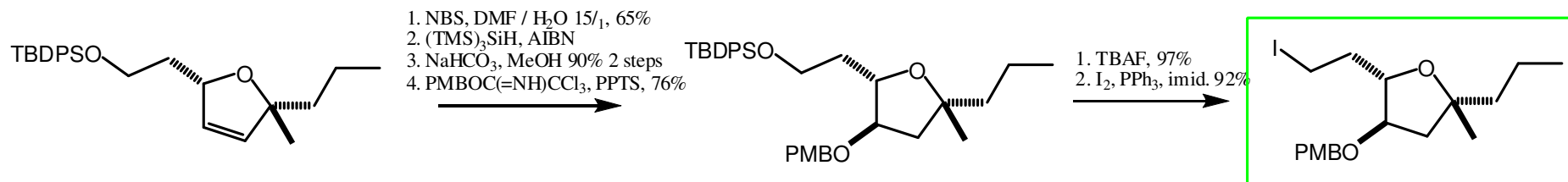
Breazzano 4 - CU Synthesis Lit Group – Amphidinolide X

Furstner Synthesis



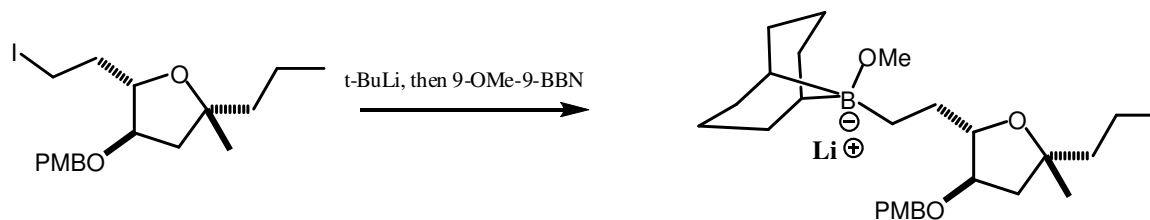
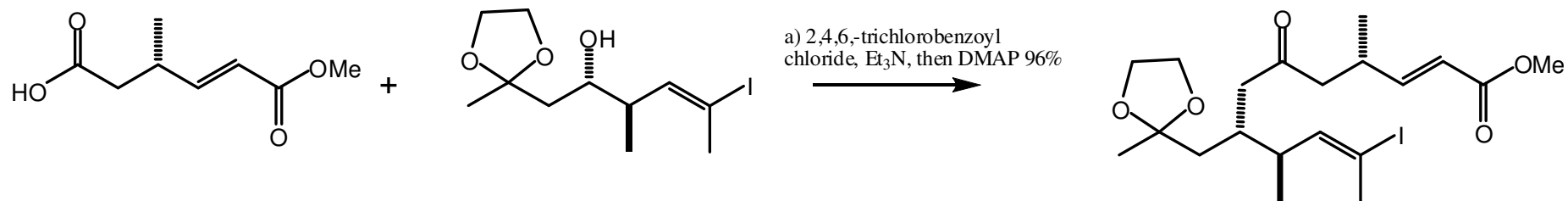
Breazzano 5 - CU Synthesis Lit Group – Amphidinolide X

Furstner Synthesis



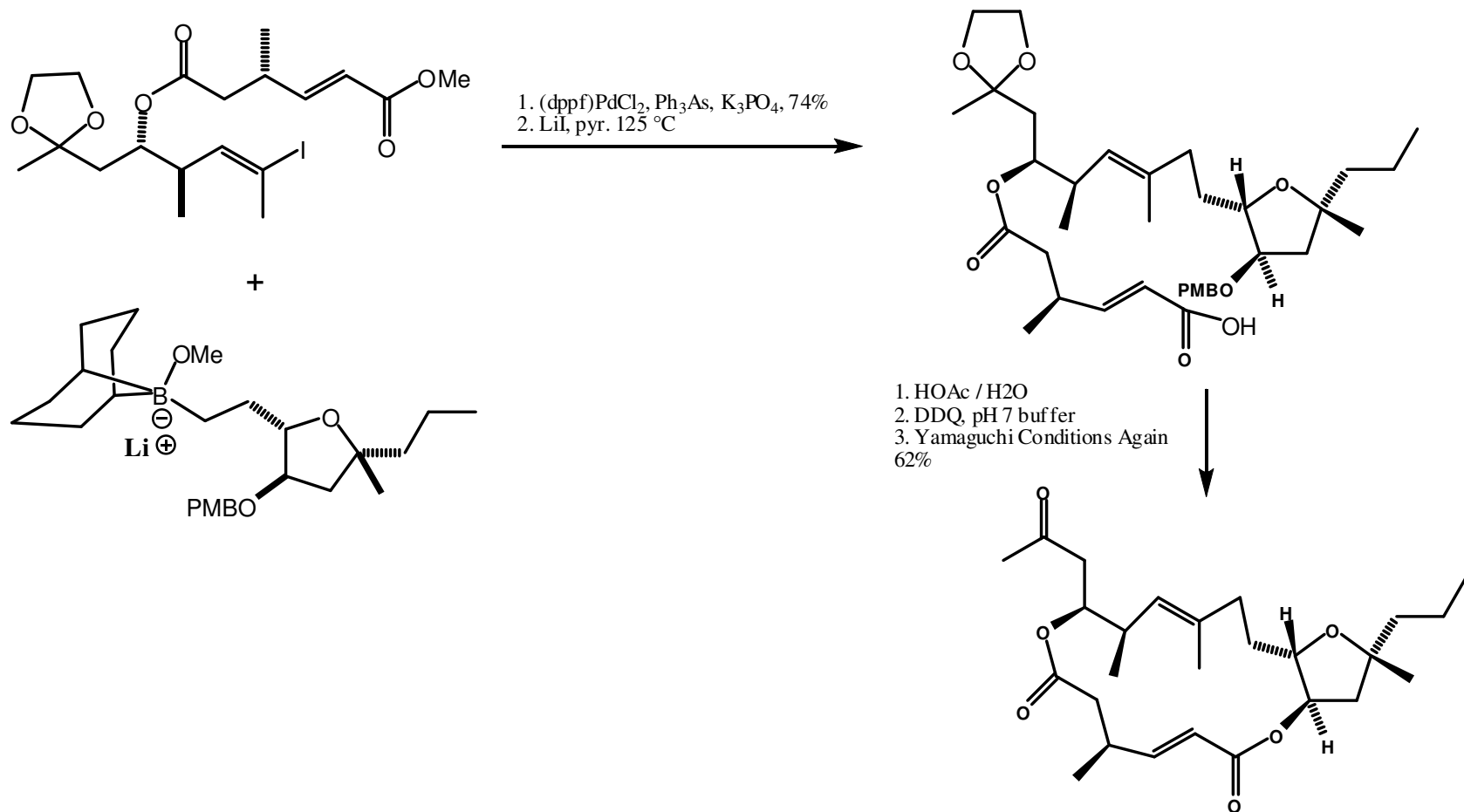
Breazzano 6 - CU Synthesis Lit Group – Amphidinolide X

Furstner Synthesis



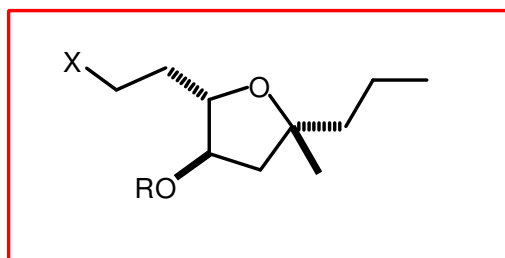
Breazzano 7 - CU Synthesis Lit Group – Amphidinolide X

Furstner Synthesis

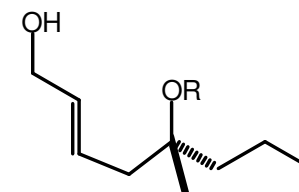
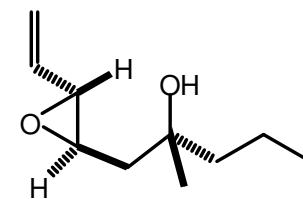
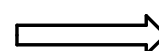
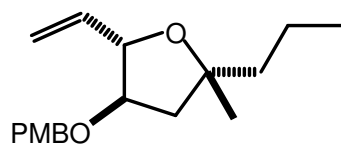
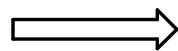


Breazzano 8 - CU Synthesis Lit Group – Amphidinolide X

Dai's THF Synthesis

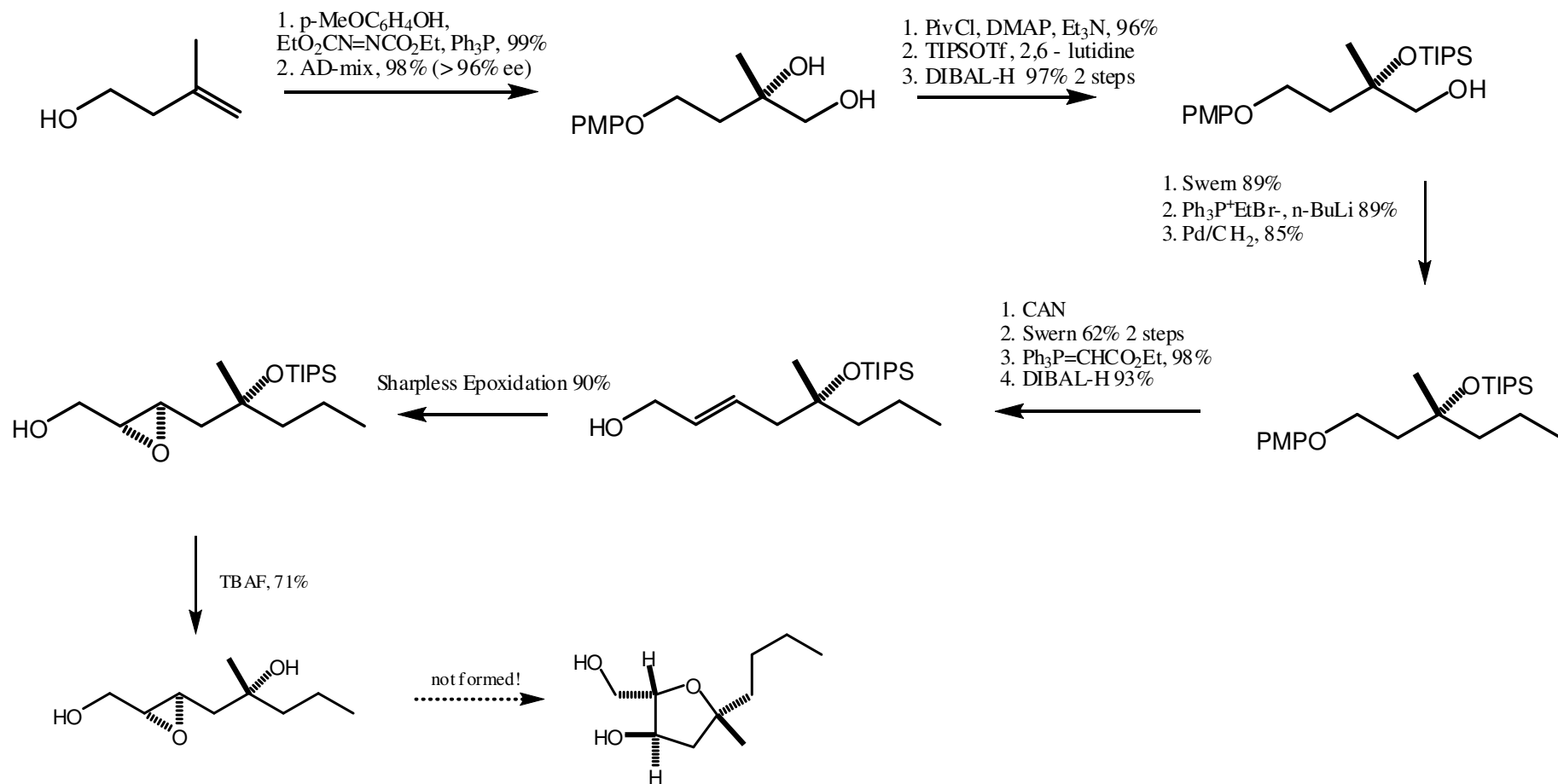


Furstner THF



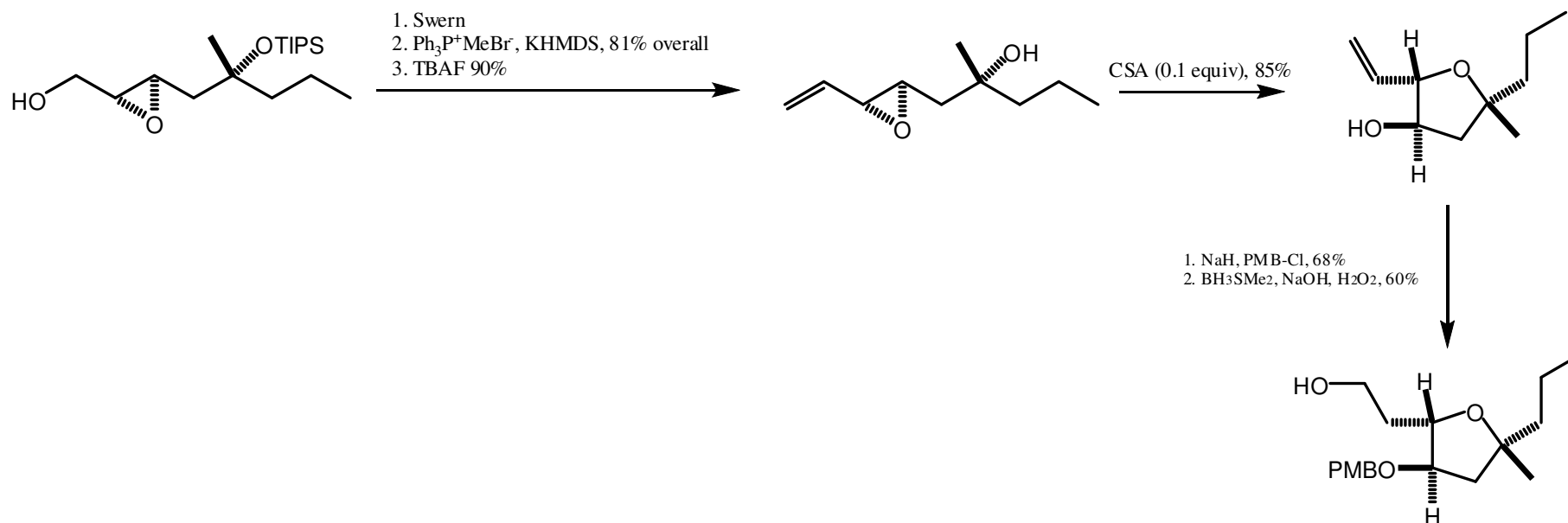
Breazzano 9 - CU Synthesis Lit Group – Amphidinolide X

Dai's THF Synthesis



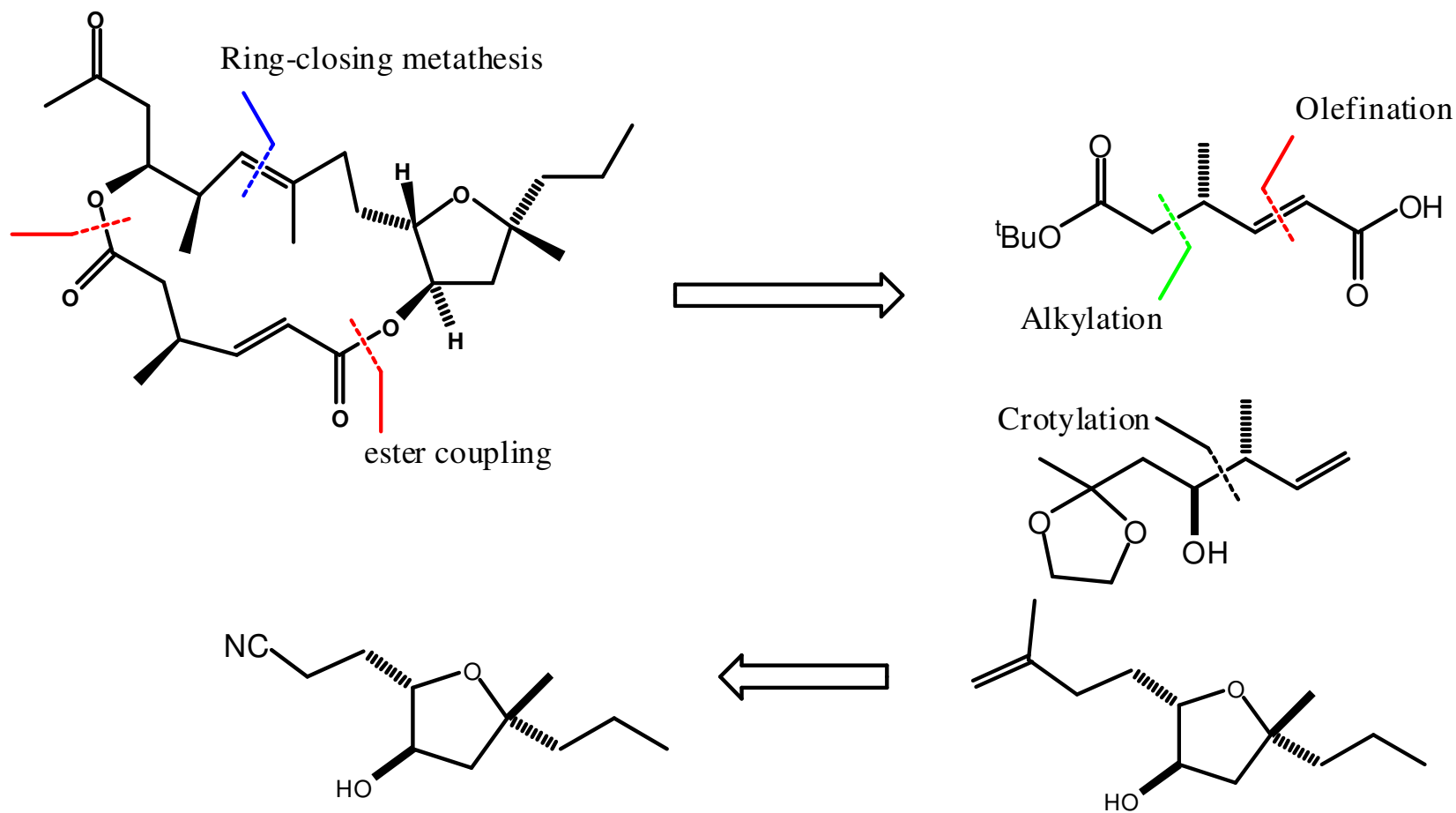
Breazzano 10 - CU Synthesis Lit Group – Amphidinolide X

Dai's THF Synthesis



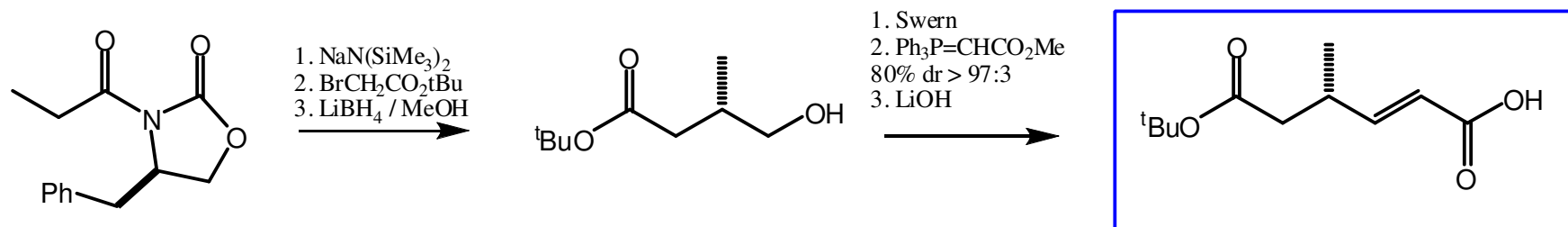
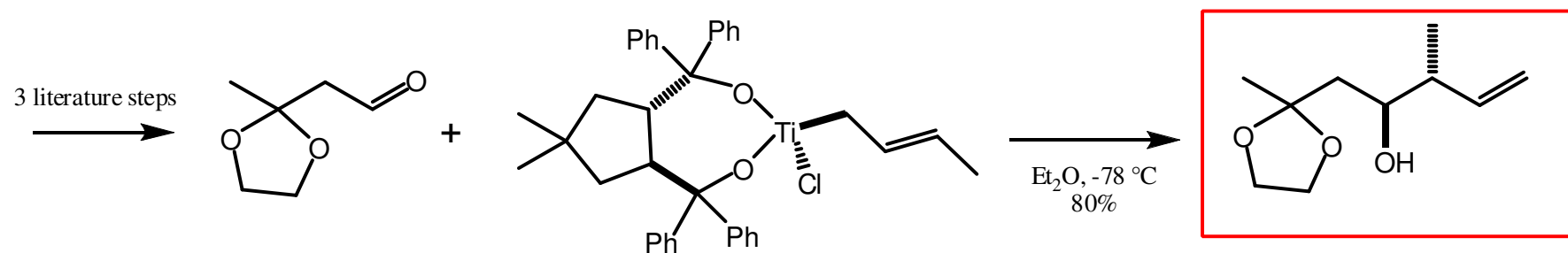
Breazzano 11 - CU Synthesis Lit Group – Amphidinolide X

Vilarrasa's Synthesis



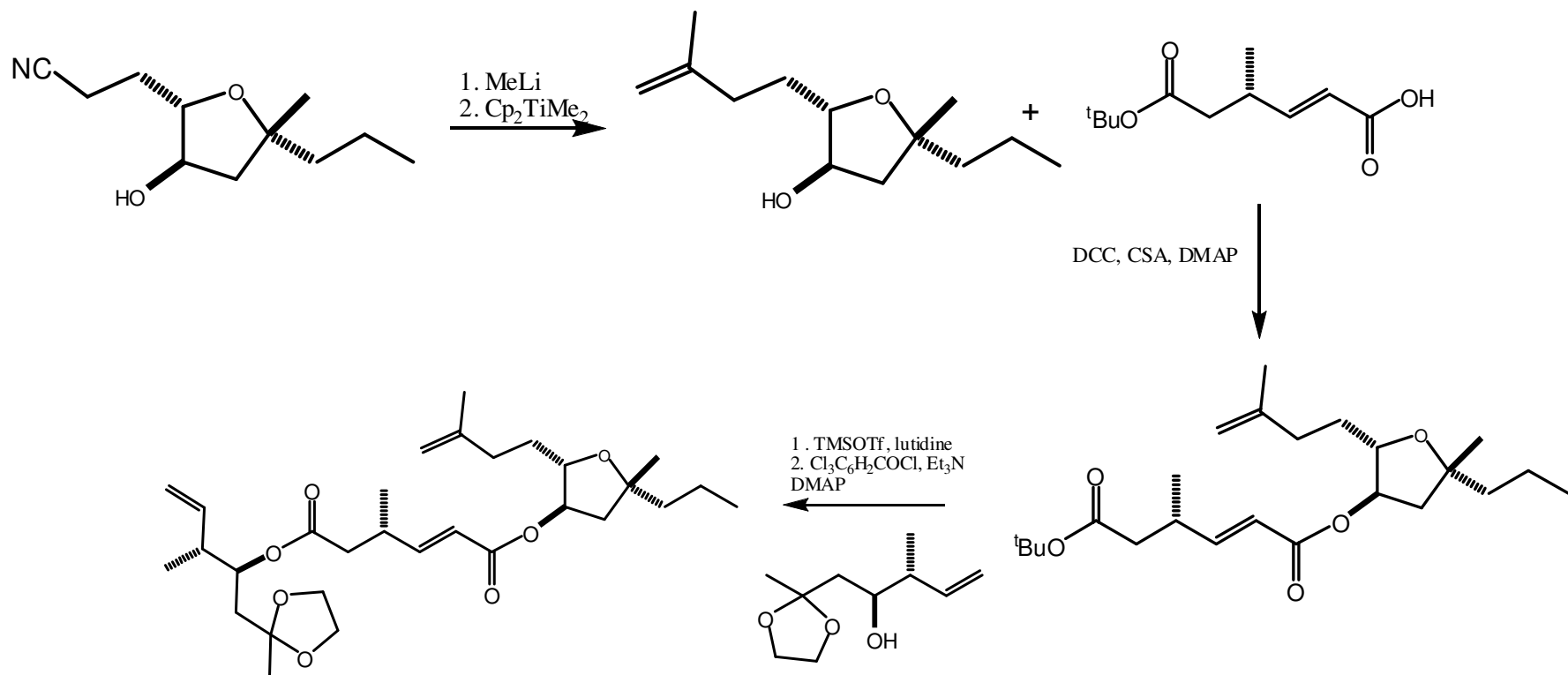
Breazzano 12 - CU Synthesis Lit Group – Amphidinolide X

Vilarrasa's Synthesis



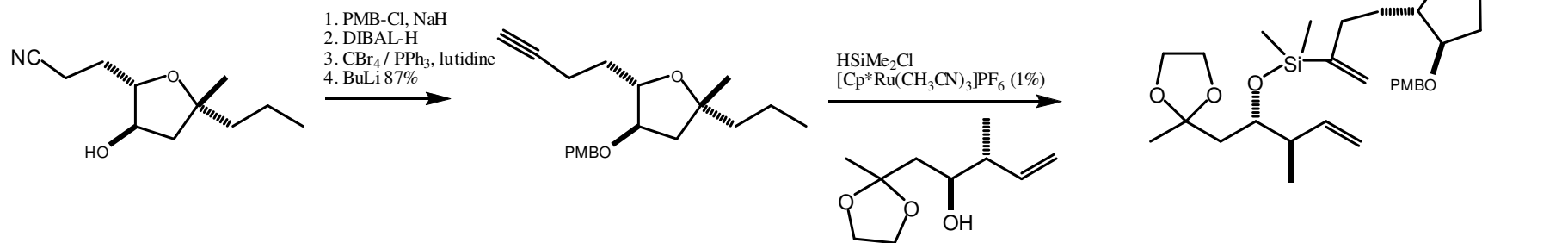
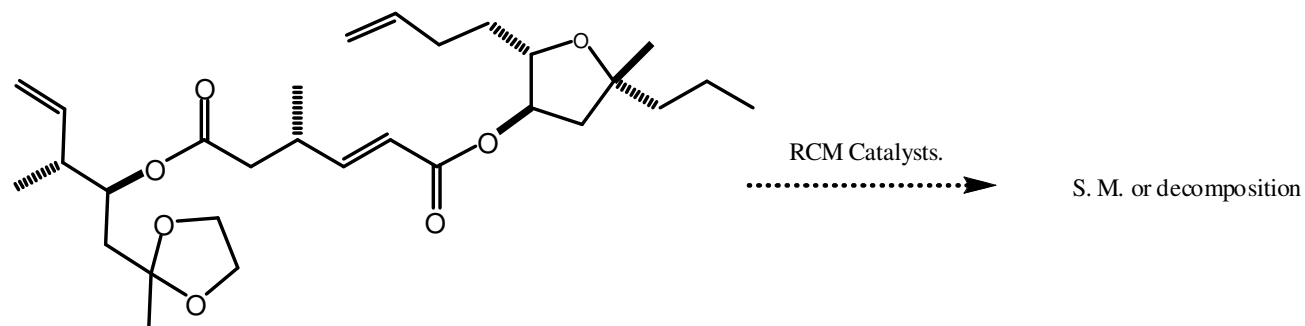
Breazzano 13 - CU Synthesis Lit Group – Amphidinolide X

Vilarrasa's Synthesis



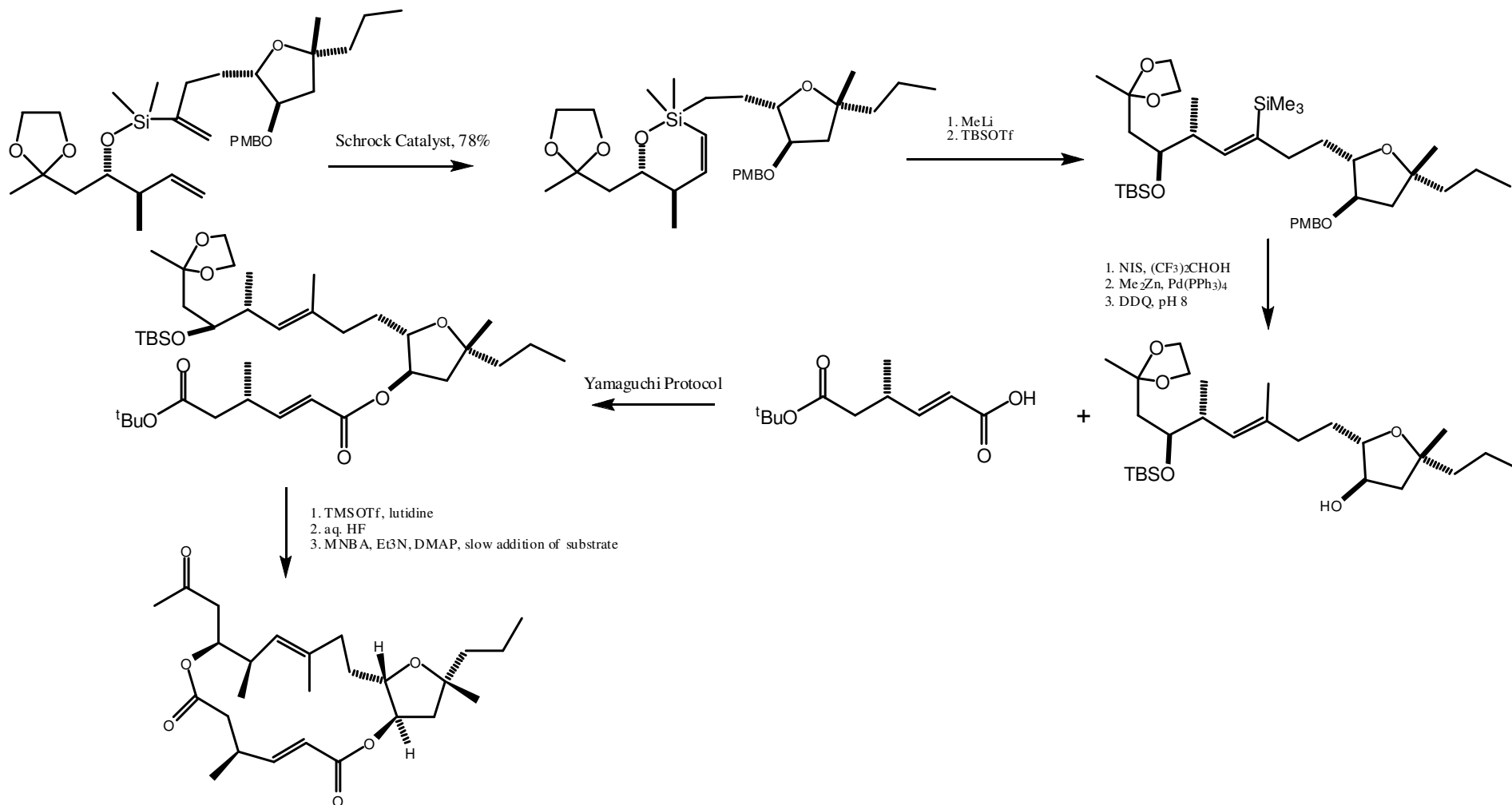
Breazzano 14 - CU Synthesis Lit Group – Amphidinolide X

Vilarrasa's Synthesis



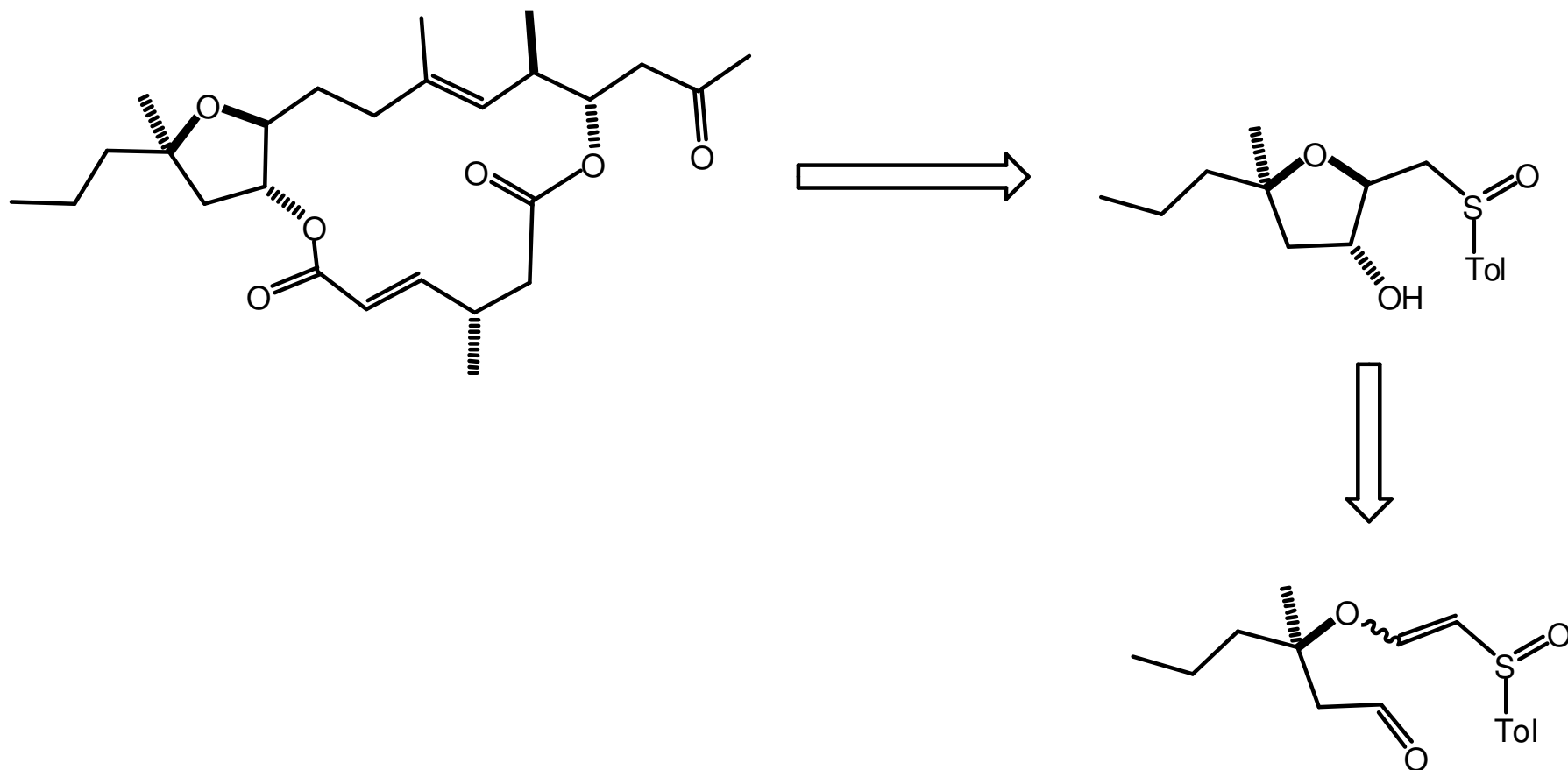
Breazzano 15 - CU Synthesis Lit Group – Amphidinolide X

Vilarrasa's Synthesis



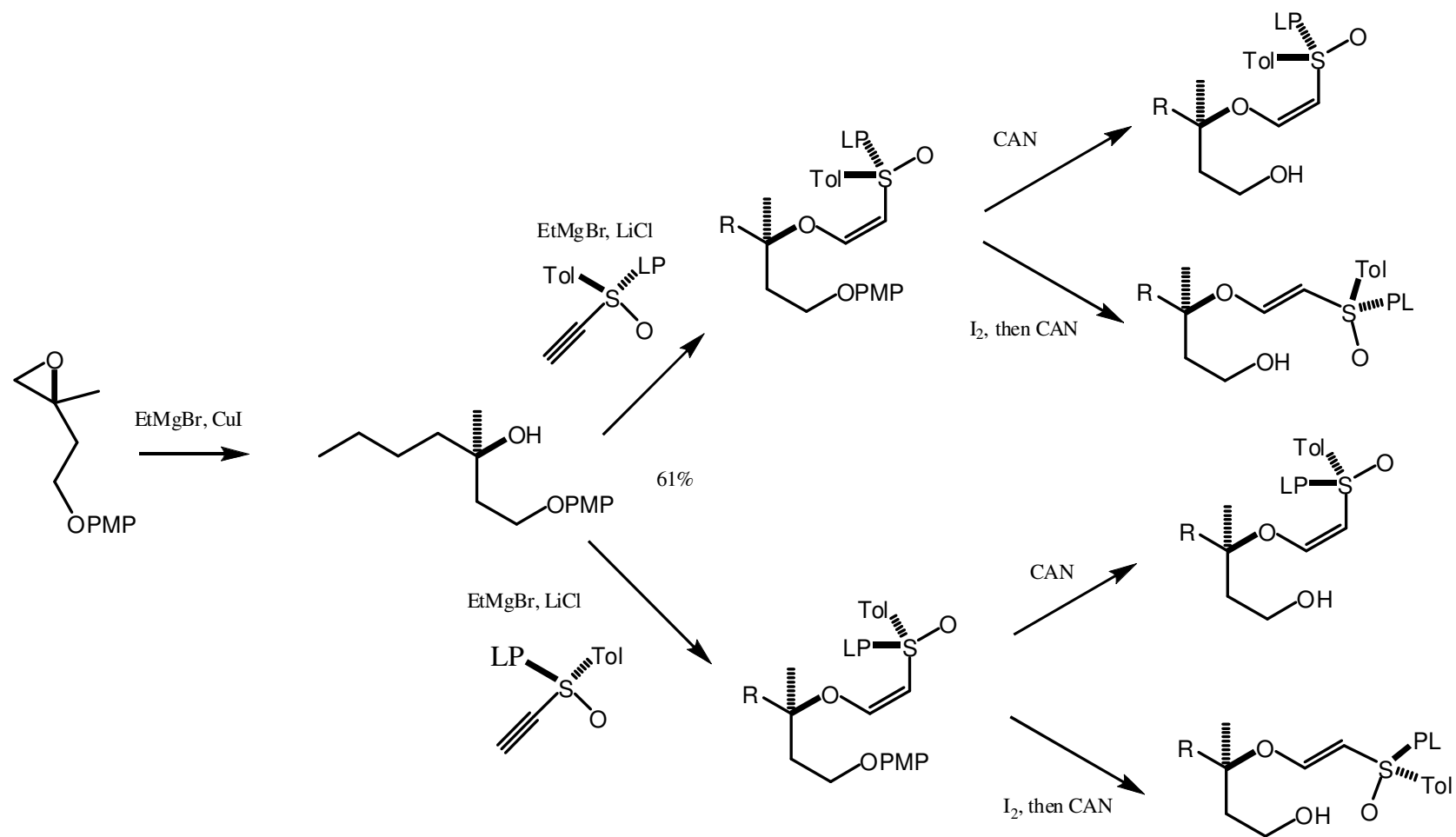
Breazzano 16 - CU Synthesis Lit Group – Amphidinolide X

Lee's Synthesis



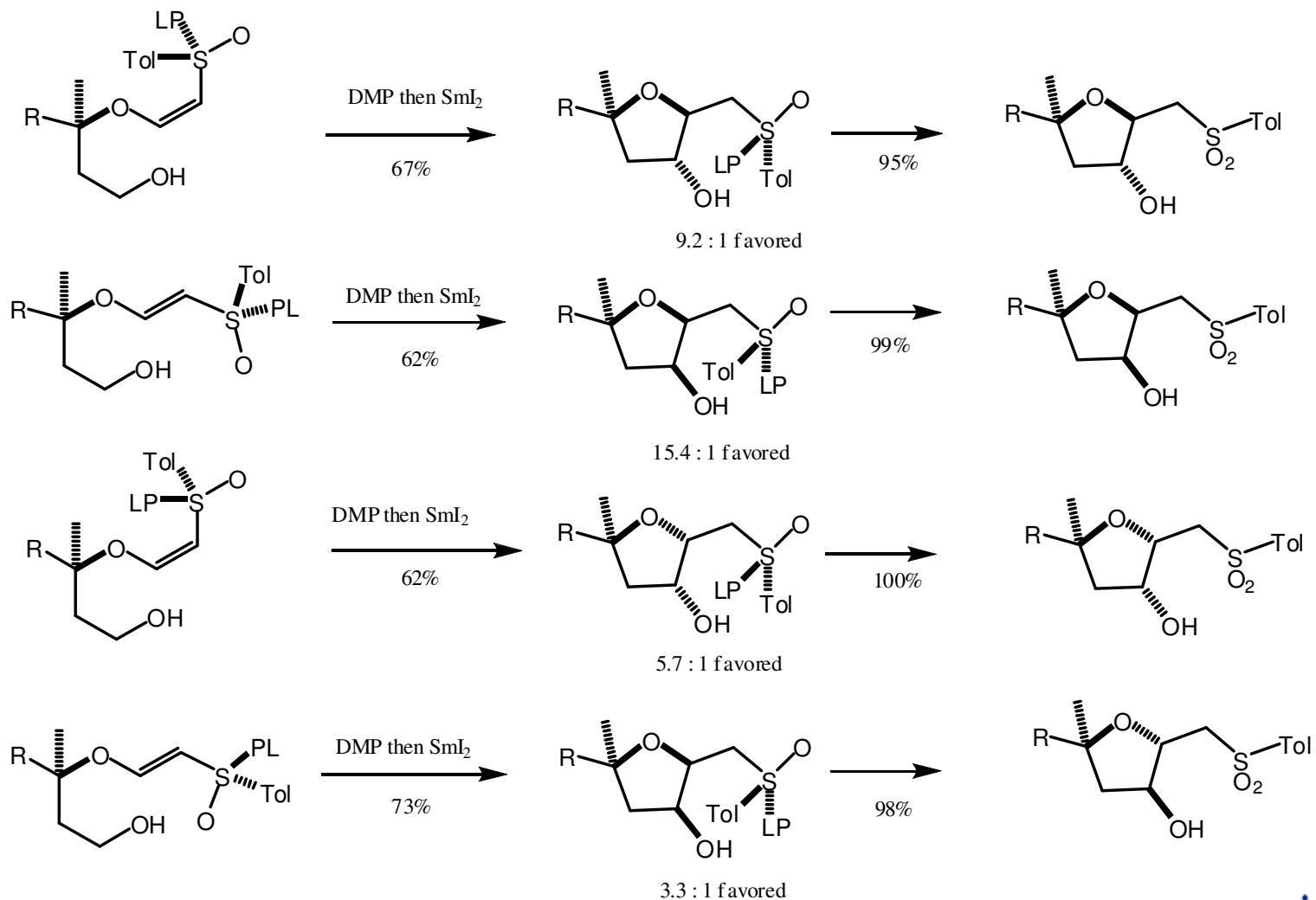
Breazzano 17 - CU Synthesis Lit Group – Amphidinolide X

Lee's Synthesis



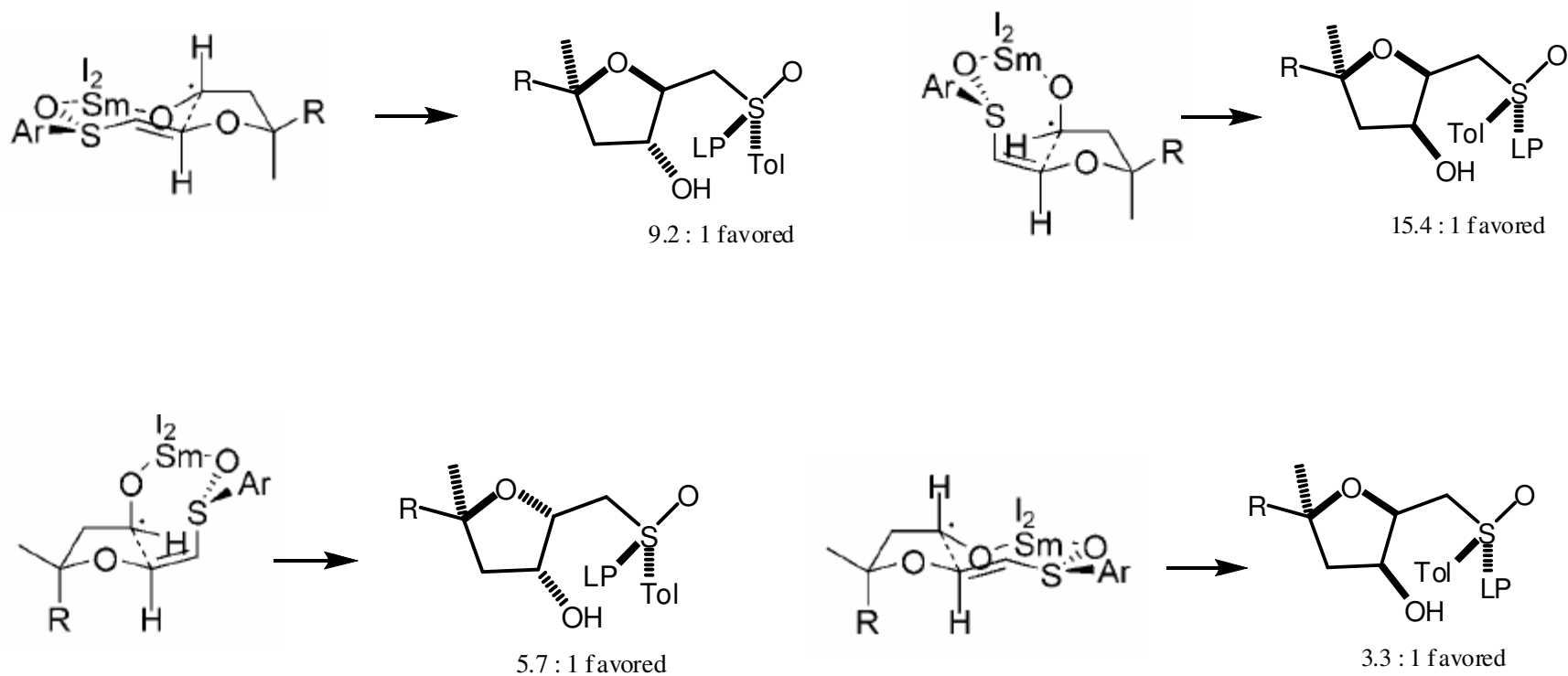
Breazzano 18 - CU Synthesis Lit Group – Amphidinolide X

Lee's Synthesis



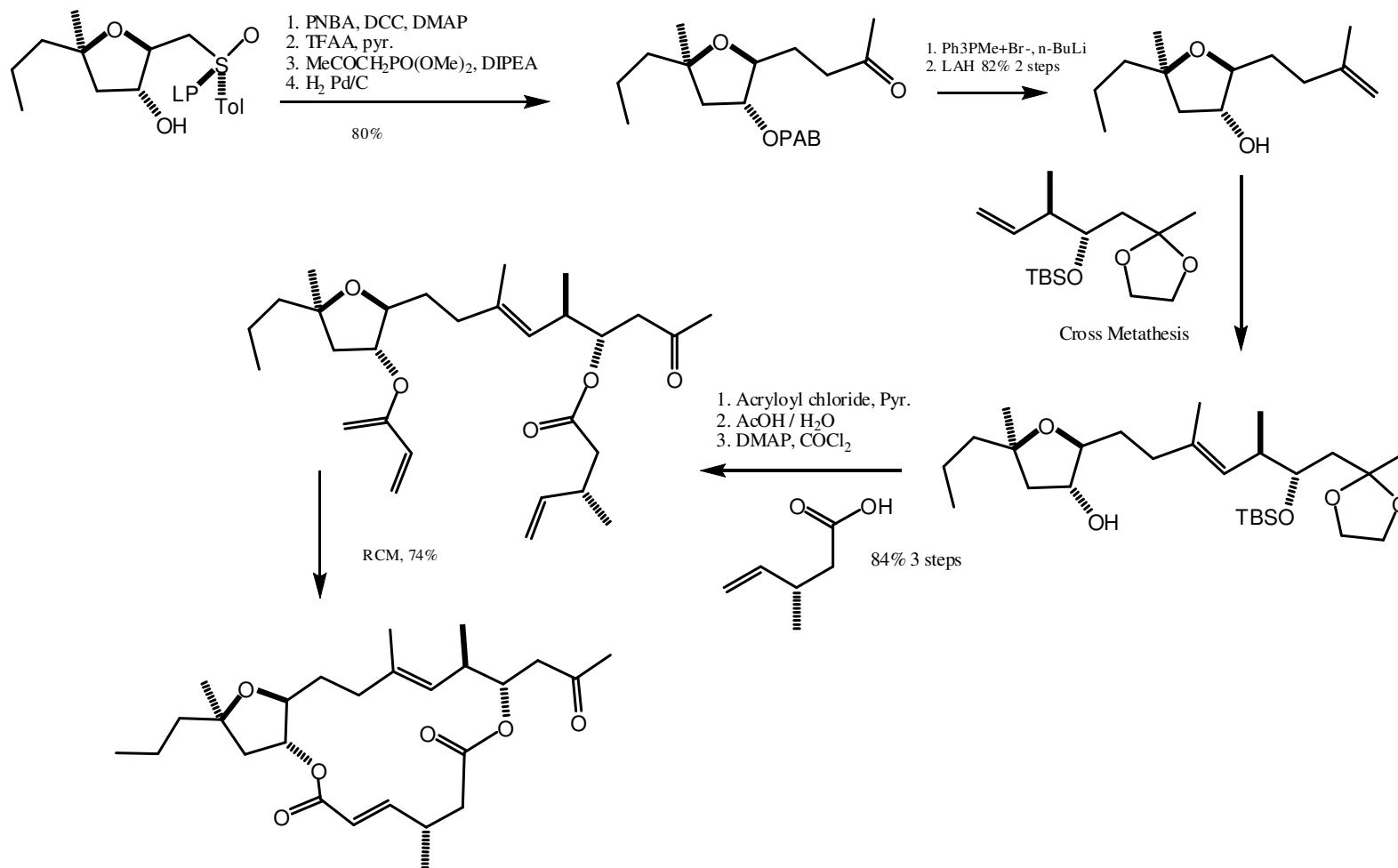
Breazzano 19 - CU Synthesis Lit Group – Amphidinolide X

Lee's Synthesis



Breazzano 20 - CU Synthesis Lit Group – Amphidinolide X

Lee's Synthesis



Breazzano 21 - CU Synthesis Lit Group – Amphidinolide X

Final Comments

- Furstner
 - First reported, enantioselective
 - Highly convergent
 - Neat iron catalyzed addition
- Dai Synthesis
 - Formal synthesis, enantioselective
 - High step count, cool THF formation
- Vilarassa Synthesis
 - Silyl-tethered ring-closing metathesis reaction, enantioselective
 - Lee Synthesis
 - Expedient, readily prepared analogs, novel oxacycle formation, enantioselective