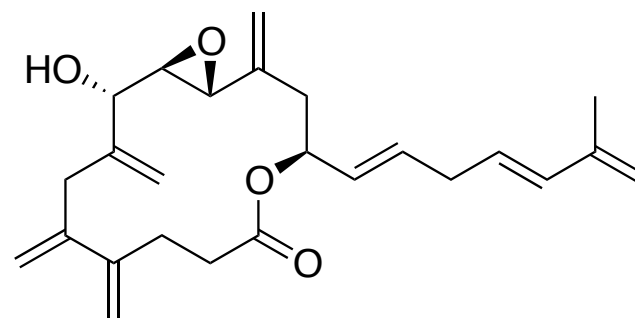


Introduction

- From plankton: Marine Dinoflagellate *Amphidinium sp* (2000)¹
- First enantioselective total synthesis by Fürstner (2007)²

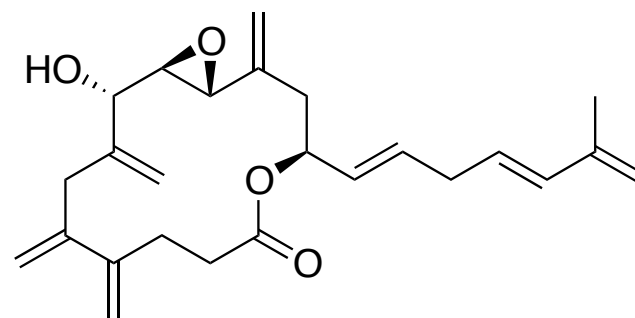


¹ Kubota, T.; Tsuda, M.; Kobayashi, J. *Tetrahedron Lett.* **2000**, 41, 713.

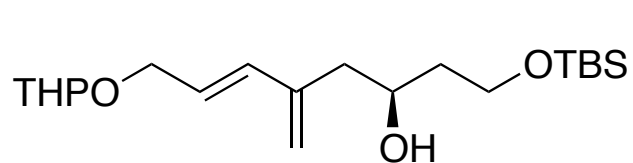
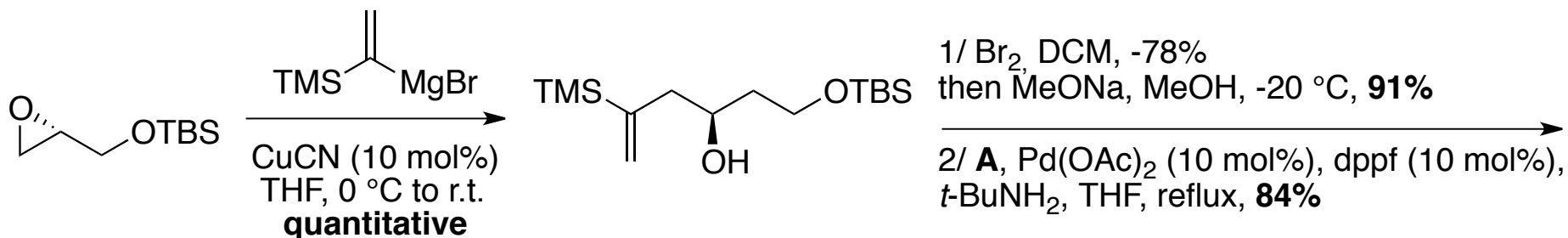
² Fürstner, A.; Larionov, O.; Flügge, S. *Ang. Chem. Int. Ed.* **2007**, 46, 5545.

Introduction

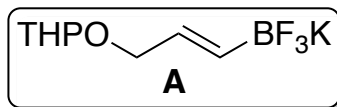
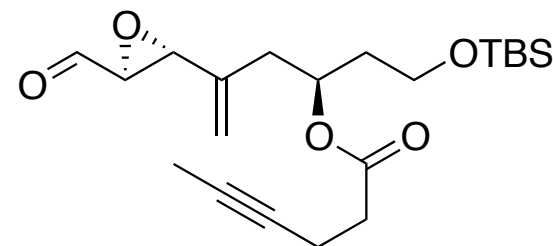
- 14-membered macrolactone
- 4 exocyclic methylene groups
- 4 asymmetric centers
(8R, 9S, 10S, 13R)
- An epoxy-alcohol
- An unsaturated-side chain



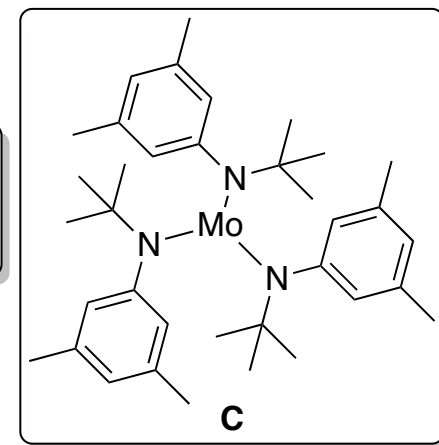
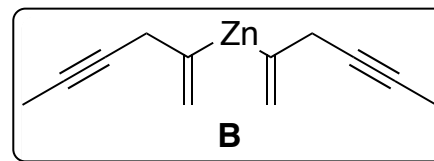
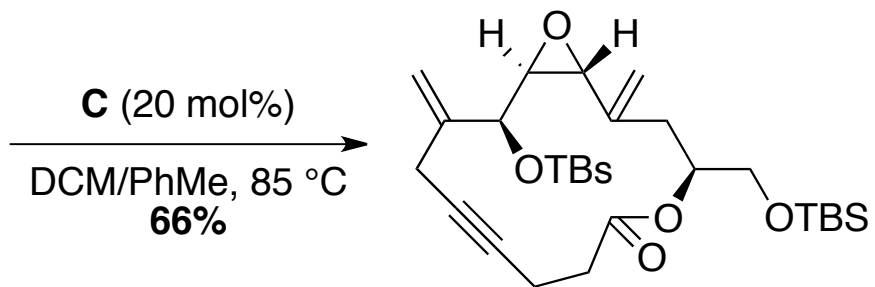
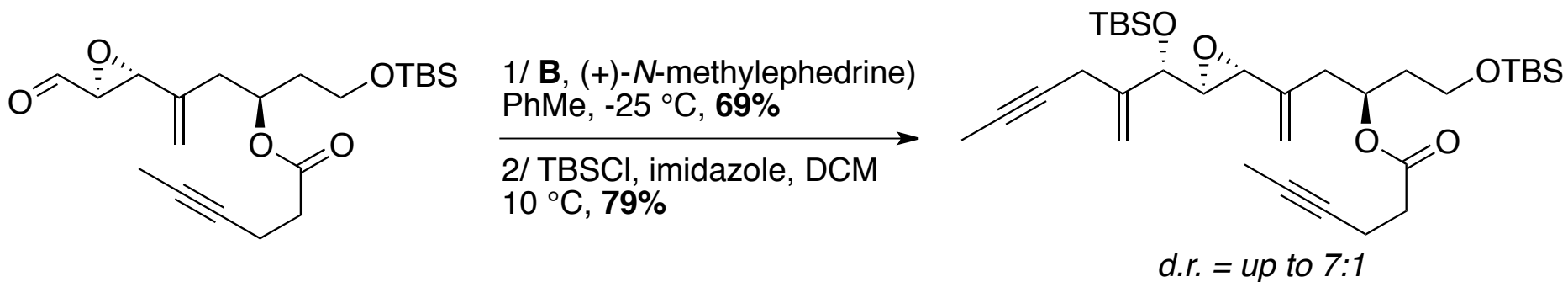
First enantioselective total synthesis



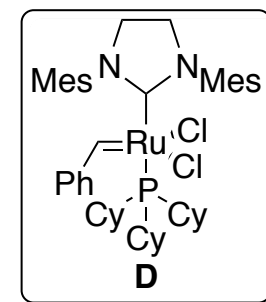
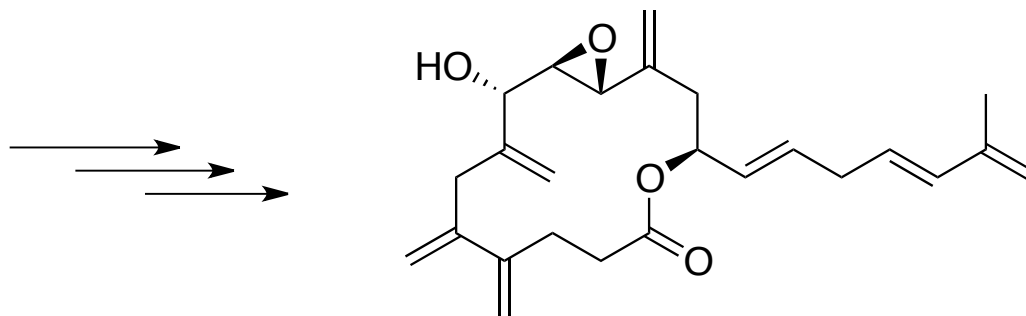
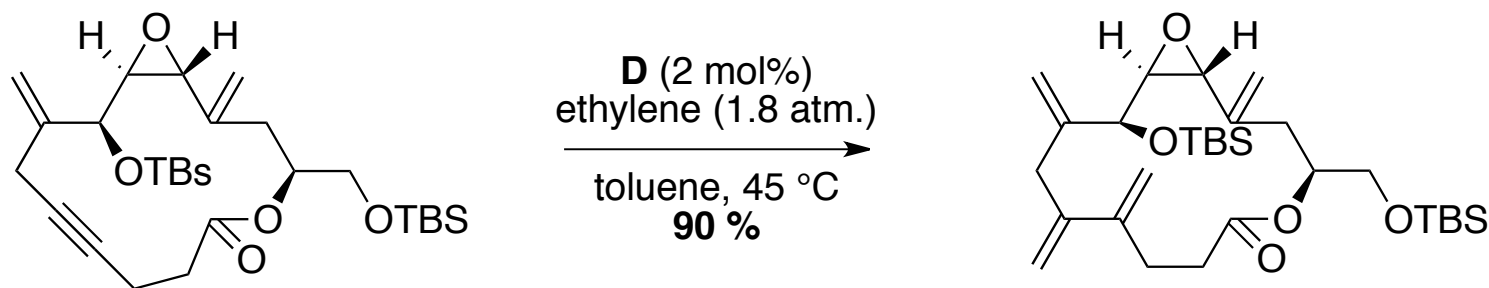
1/ Esterification
2/ deprotection
3/ Sharpless epoxidation
4/ Oxidation



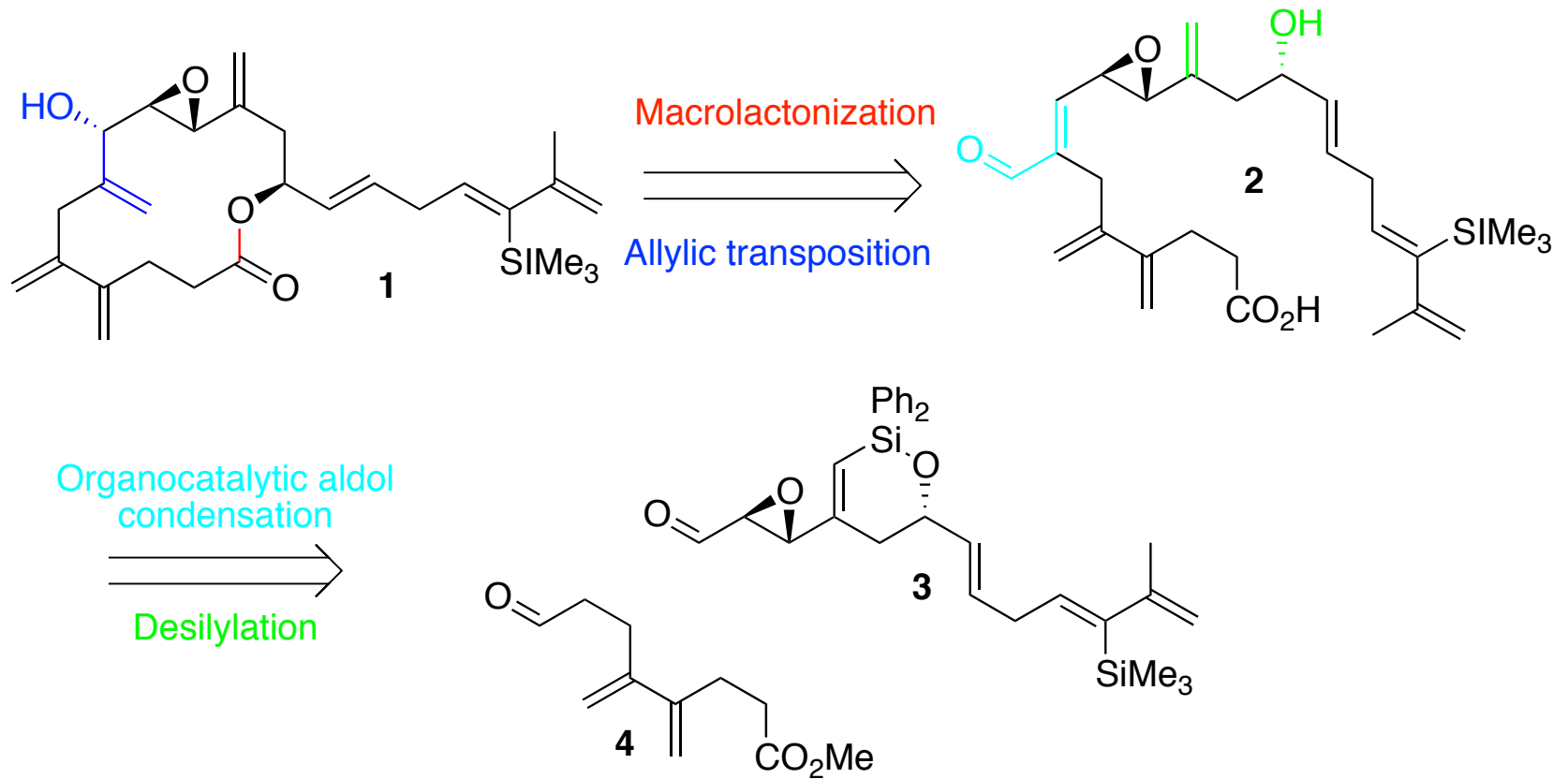
First enantioselective total synthesis



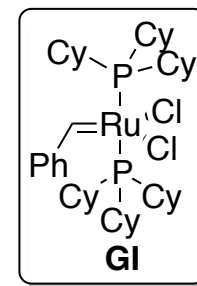
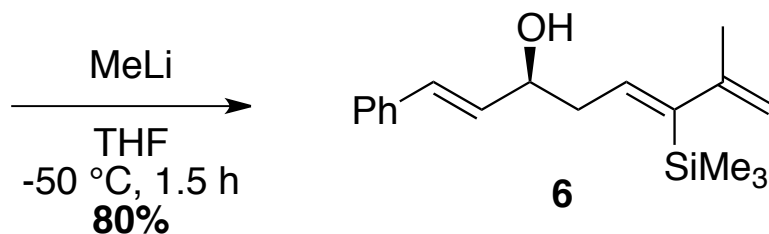
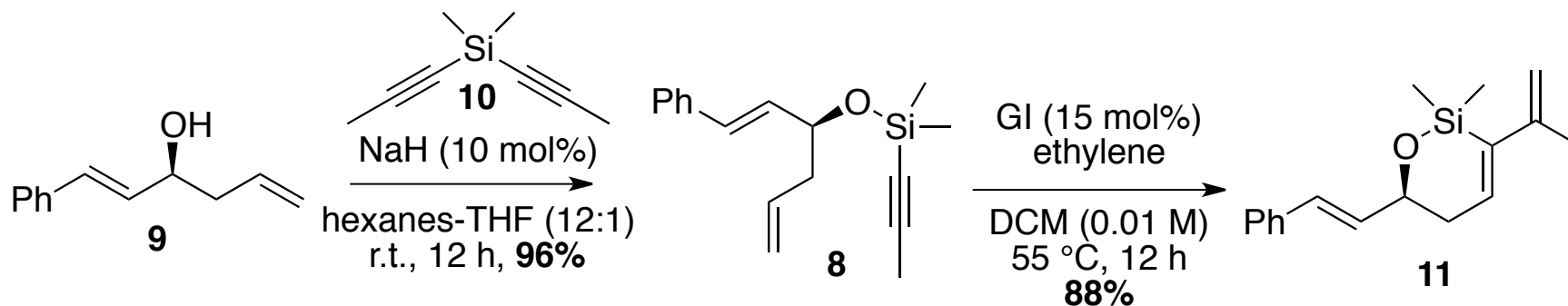
First enantioselective total synthesis



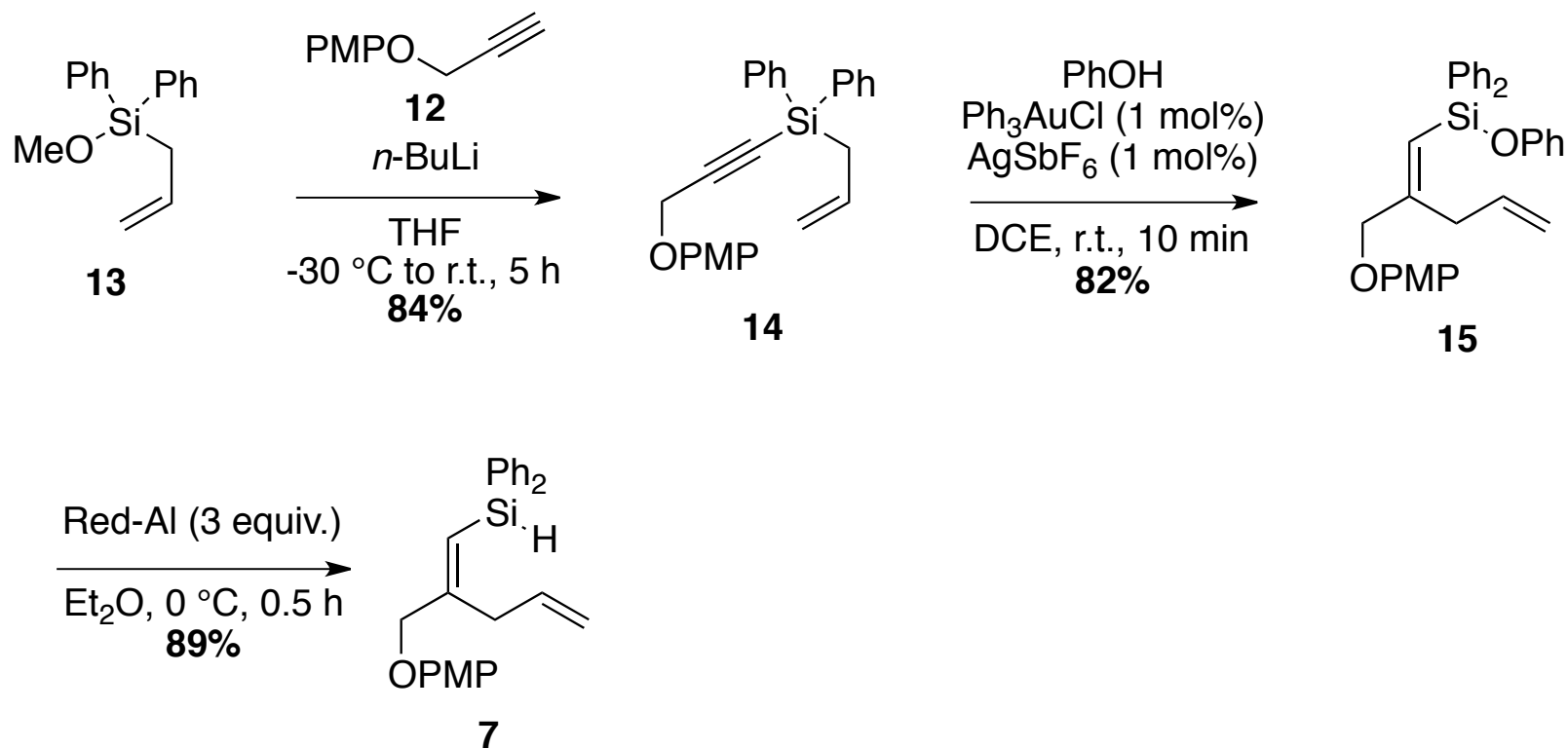
Retrosynthesis



Preparation of substrate 6

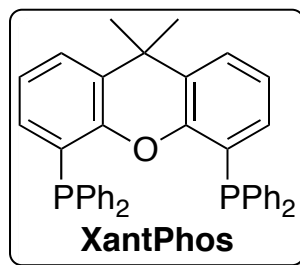
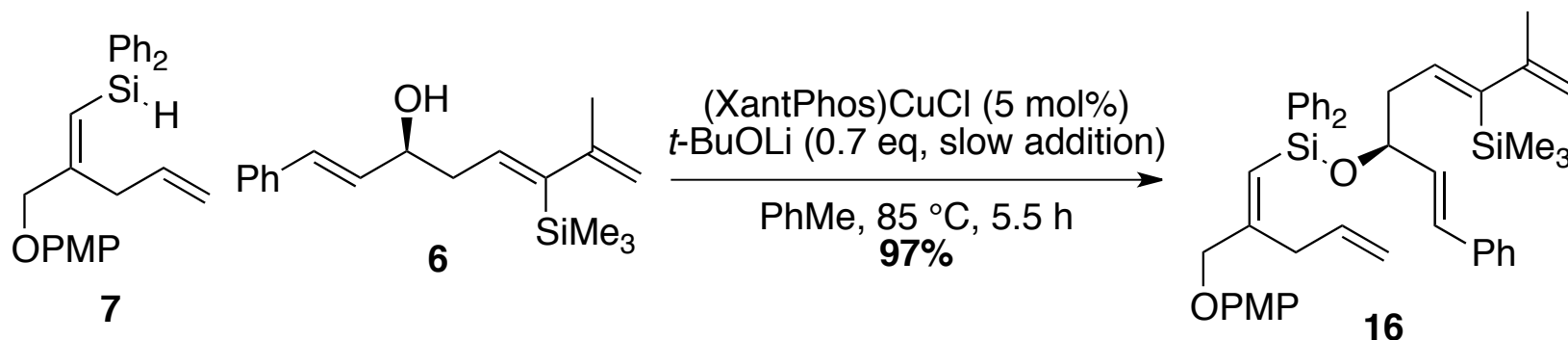


Preparation of substrate 7



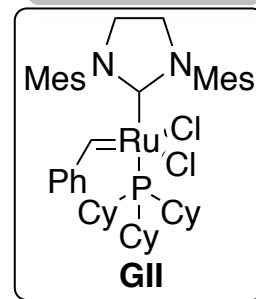
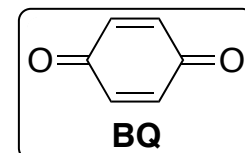
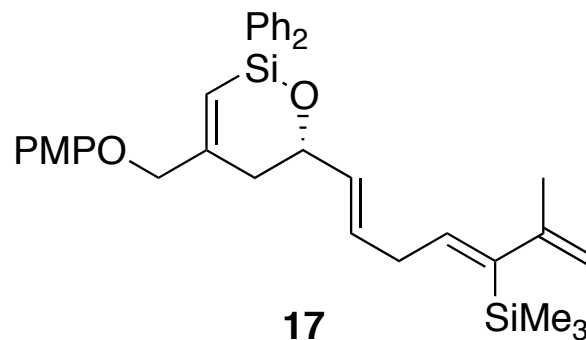
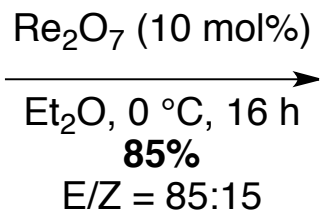
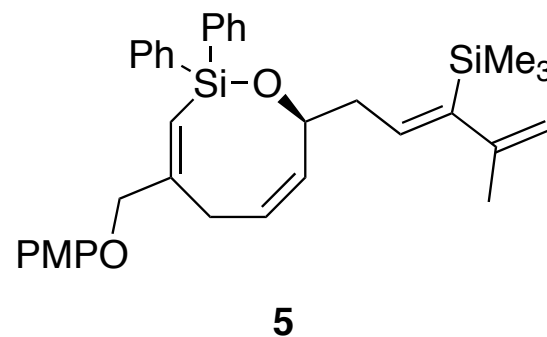
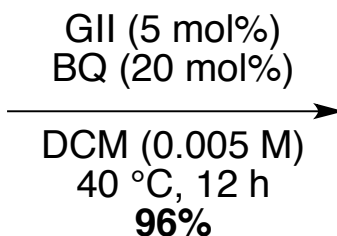
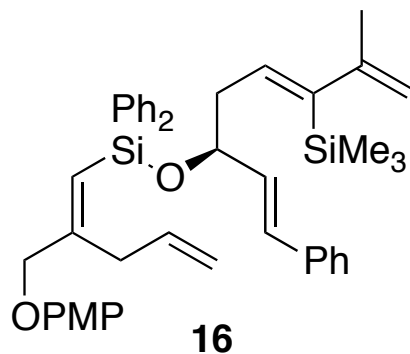
Preparation of Acceptor Aldehyde

3



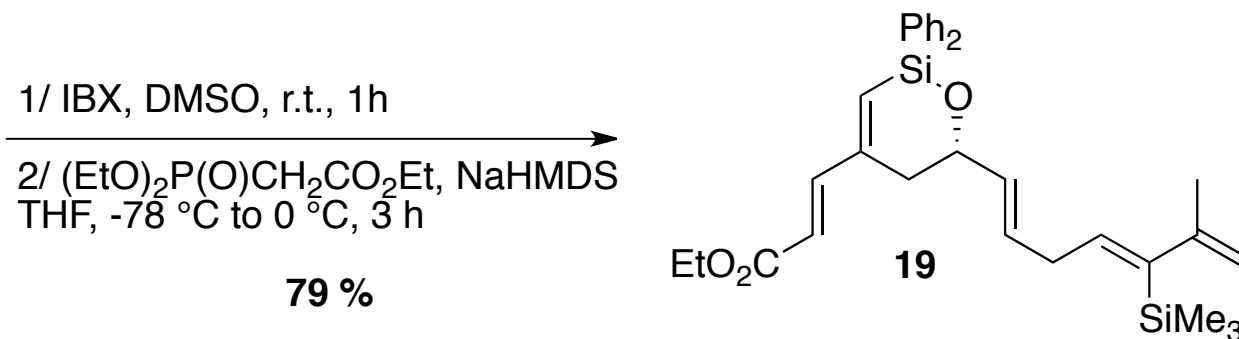
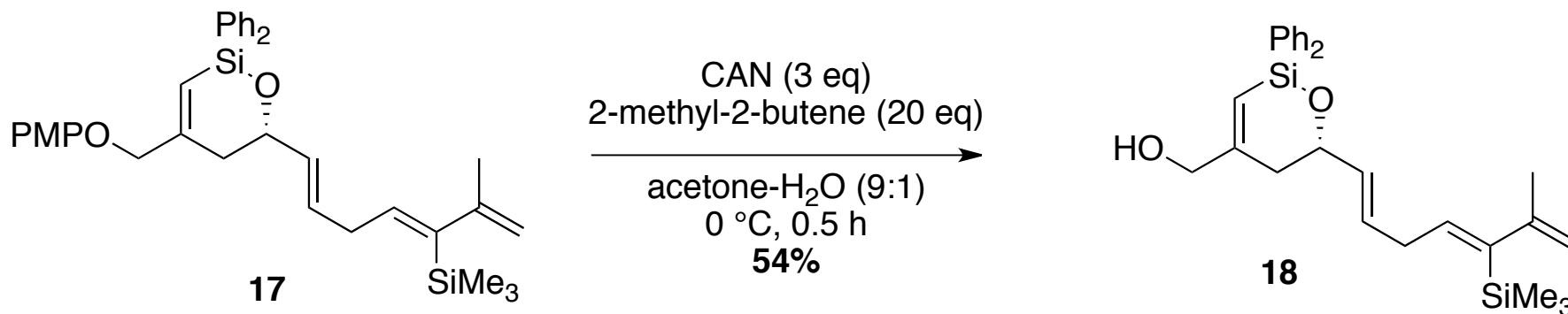
Preparation of Acceptor Aldehyde

3



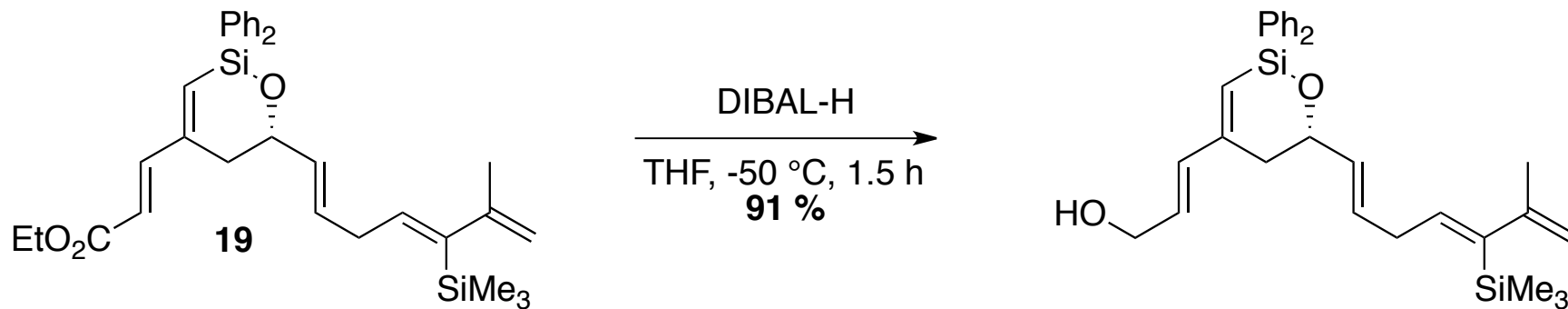
Preparation of Acceptor Aldehyde

3



Preparation of Acceptor Aldehyde

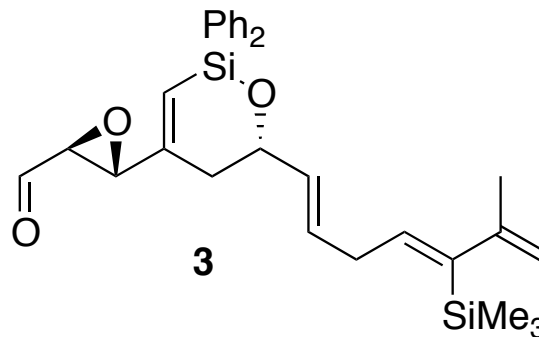
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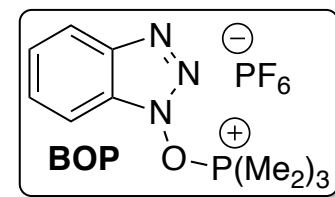
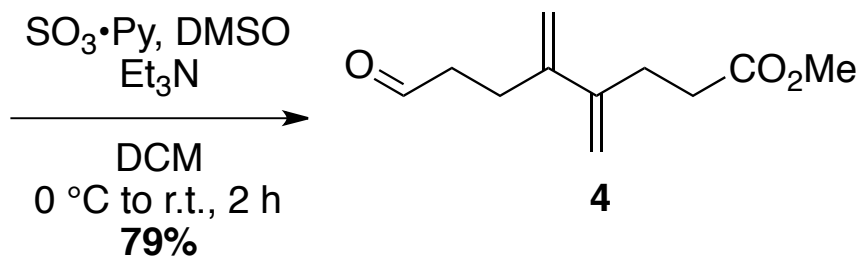
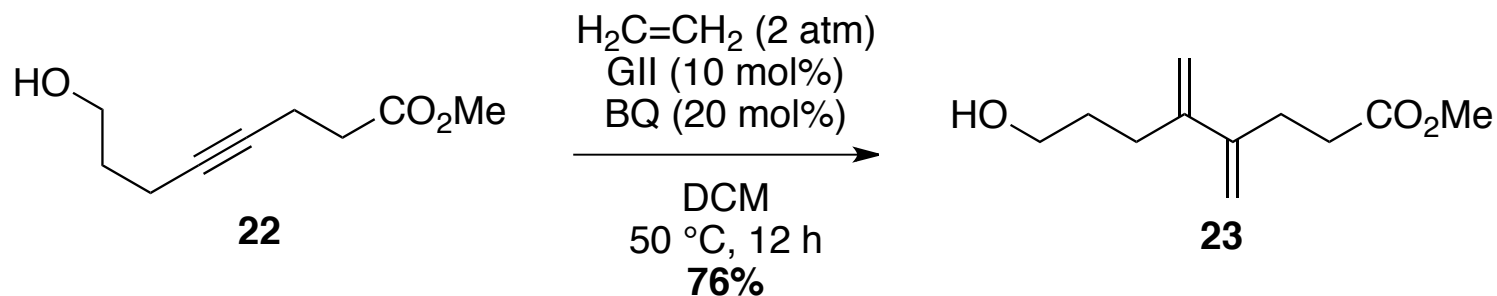
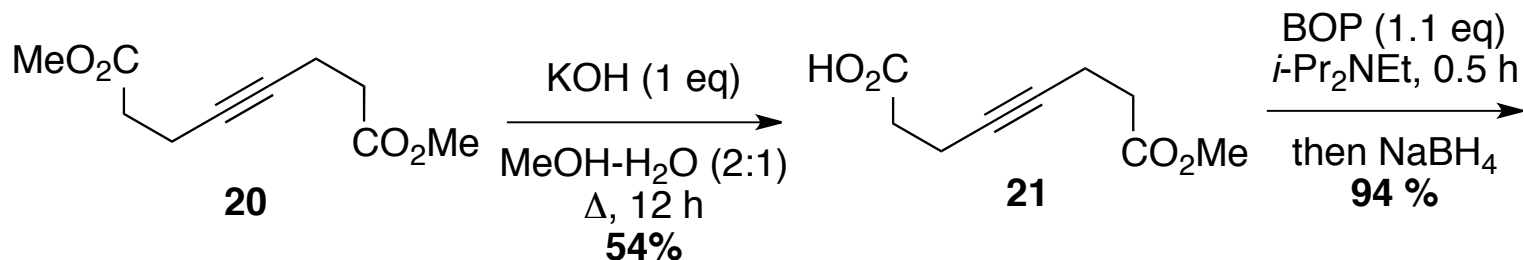
1/ $\text{Ti}(\text{O}i\text{-Pr})_4$ (10 mol%)
(-)-*D*-DIPT (15 mol%), *t*-BuOOH
MS (4 Å), DCM, $-20\text{ }^\circ\text{C}$, 12h
(d.r. = 88 :12)

2/ $\text{SO}_3 \cdot \text{Py}$, DMSO, Et_3N
DCM, $10\text{ }^\circ\text{C}$, 3 h

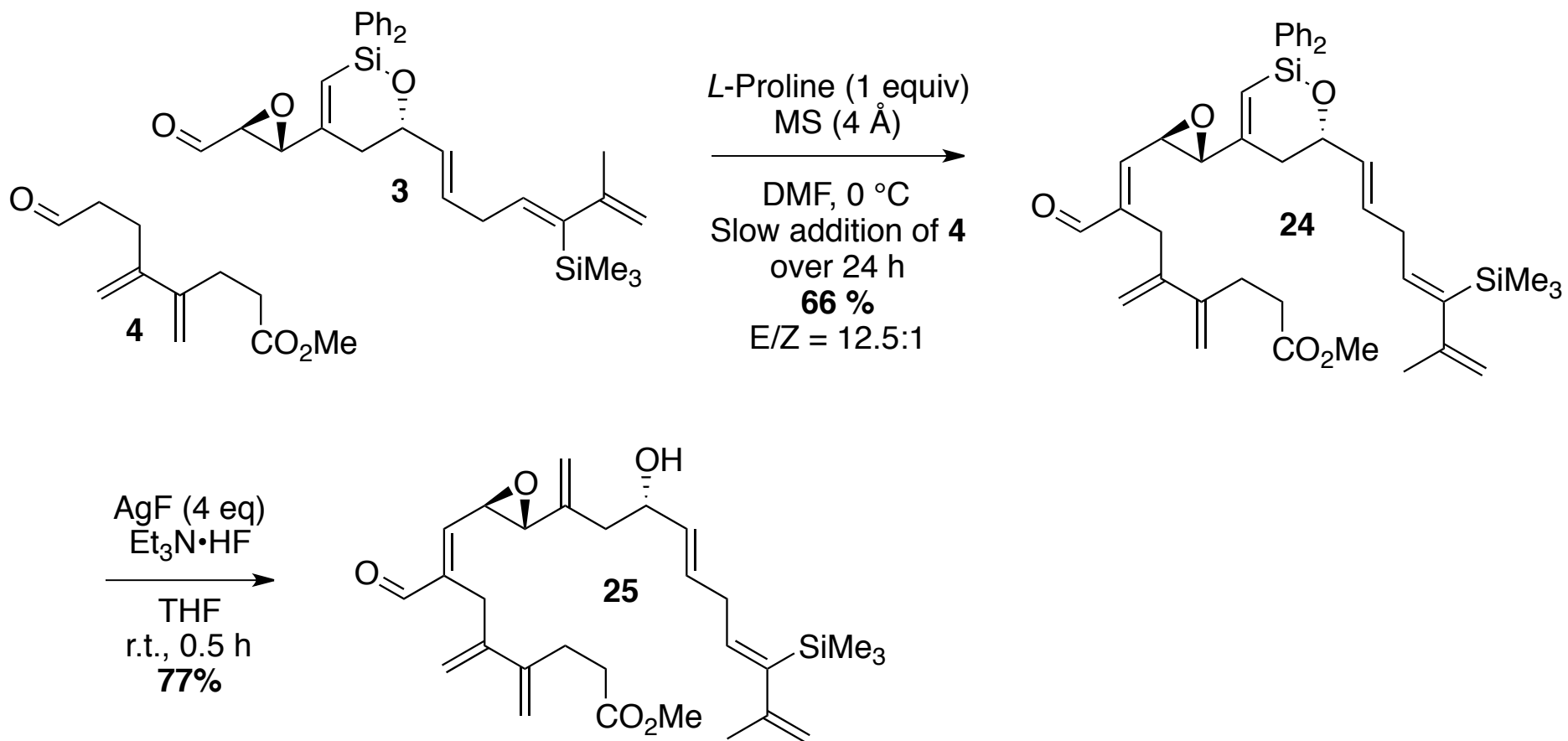
94%



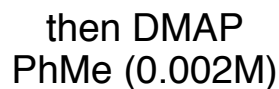
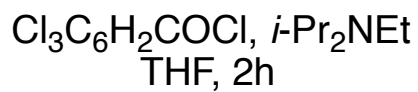
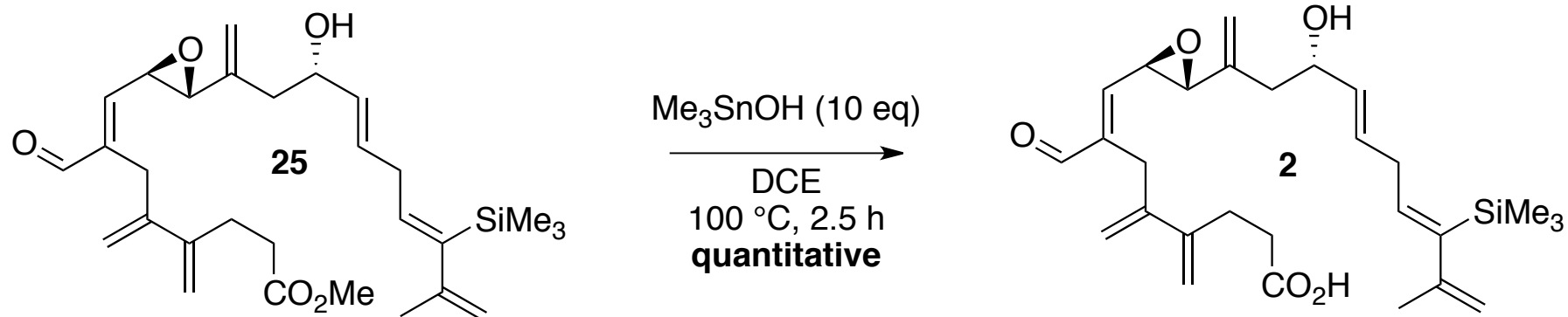
Preparation of Donor Aldehyde 4



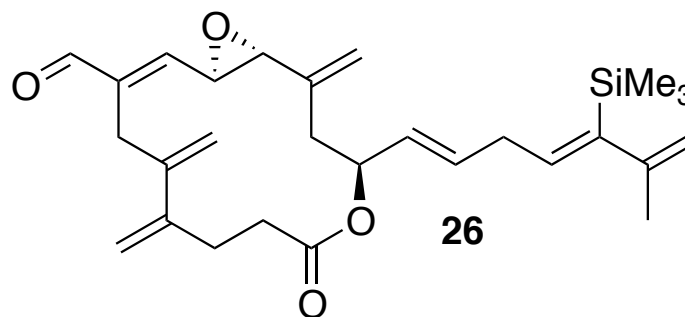
Completion of the Synthesis



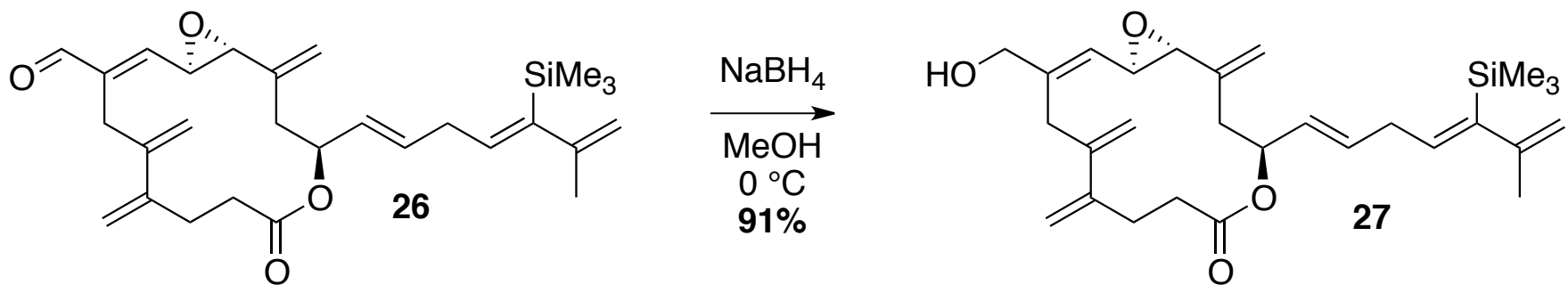
Completion of the Synthesis



61%



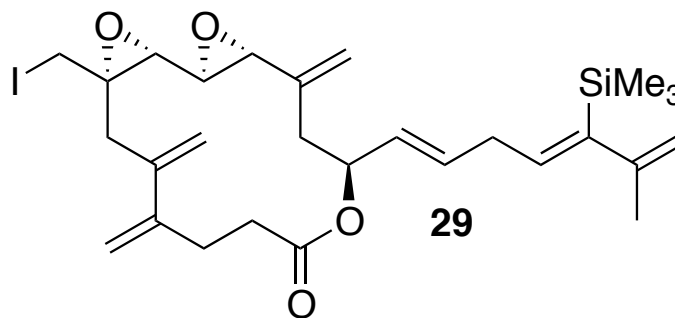
Completion of the Synthesis



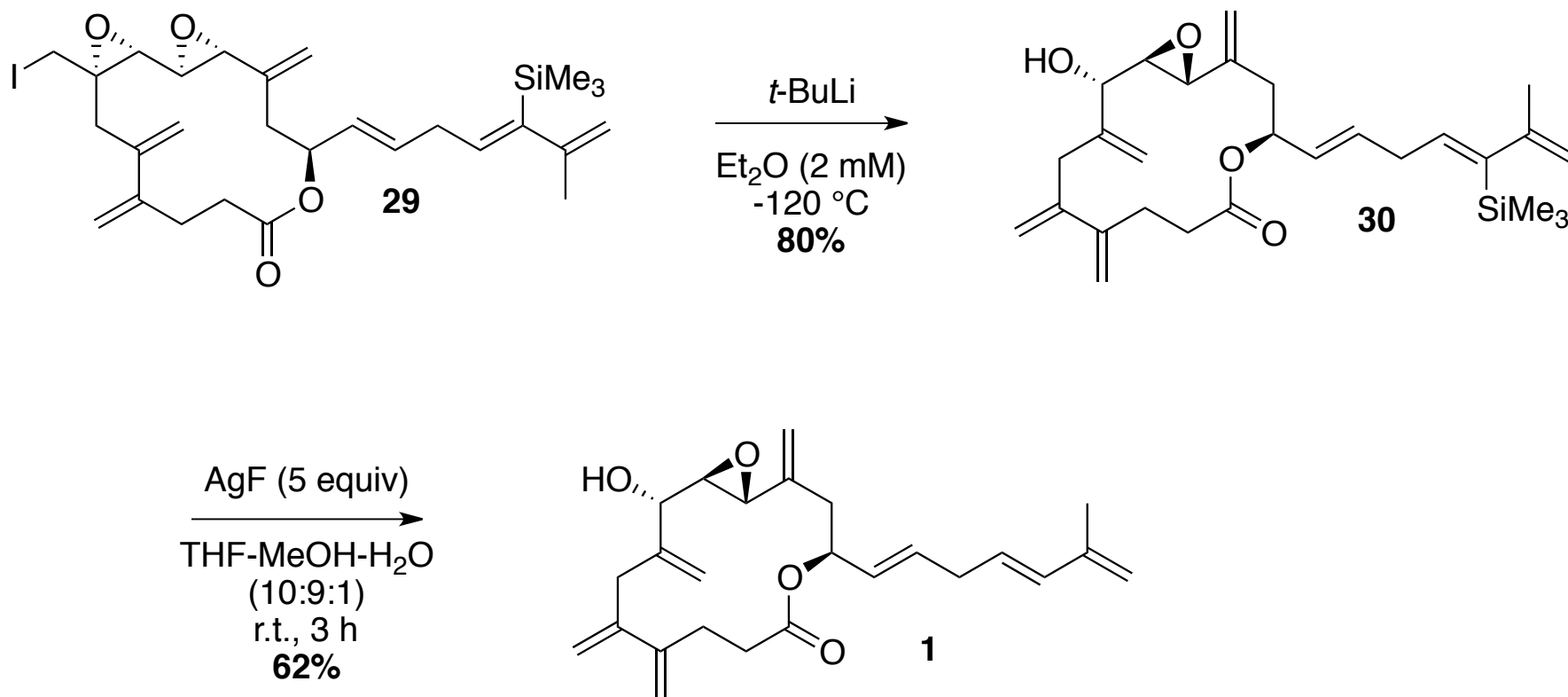
1/ Ti(O*i*-Pr)₄ (10 mol%)
(-)-*D*-DIPT (15 mol%)
t-BuOOH, MS (4 Å)
DCM, -20 °C, 12 h

2/ I₂, PPh₃, imidazole
DCM, r.t., 1.5 h

85%



Completion of the Synthesis

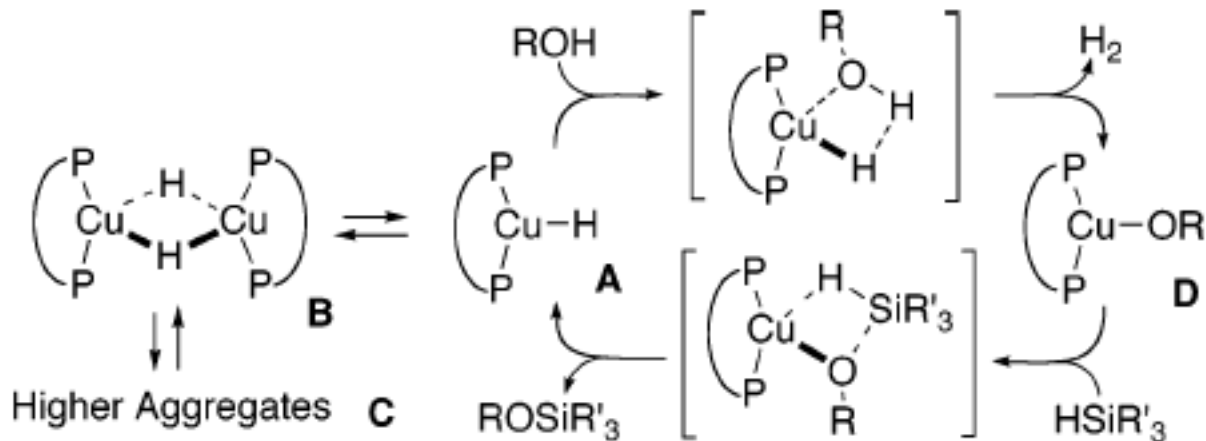


Conclusion

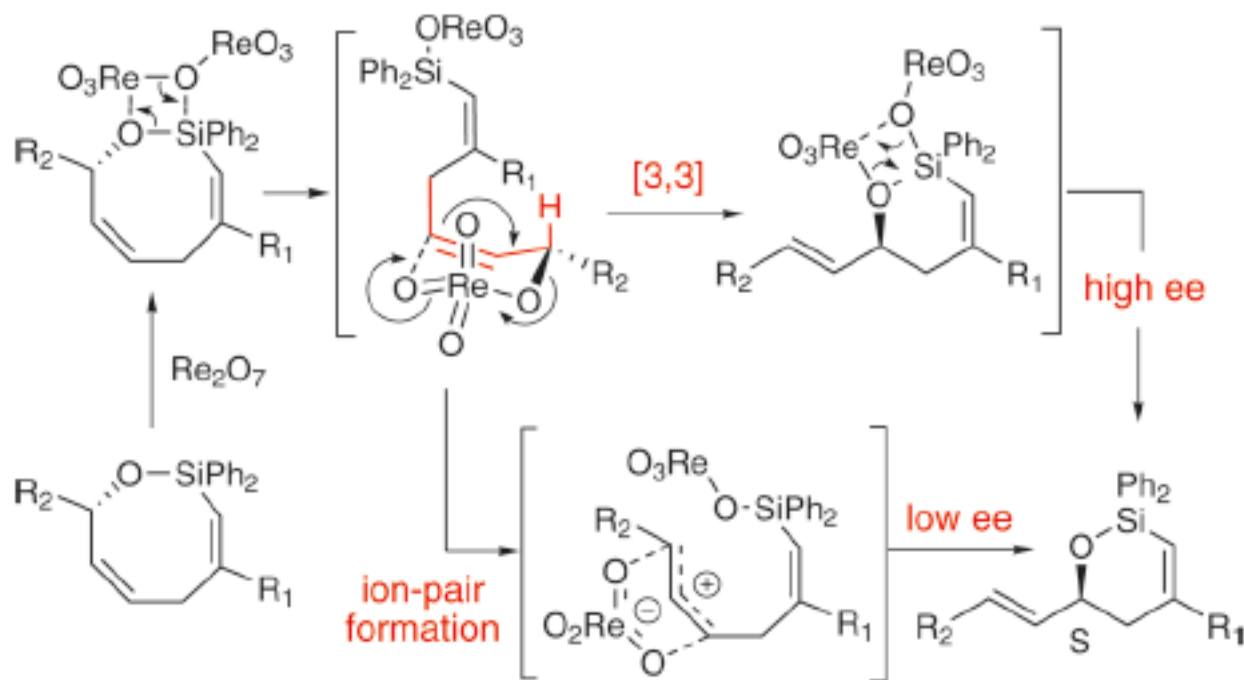
- 22 steps : overall Yield = 3.3 %
- Key steps : ring closing enyne and diene metathesis, allylic transpositions, ring contraction, cross aldol condensation

Thank you for your attention

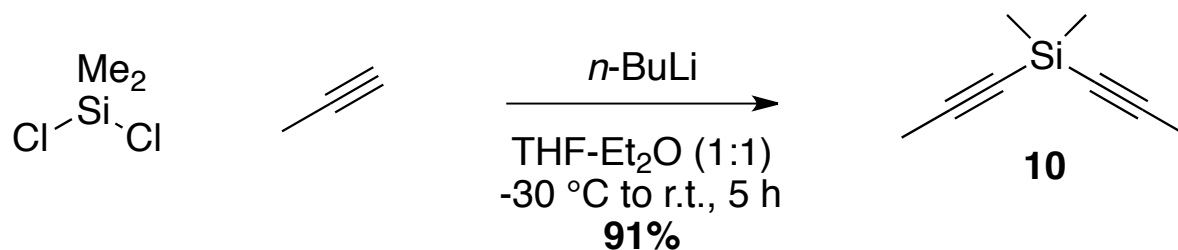
Mechanism of the Dehydrogenative Alcohol Silylation



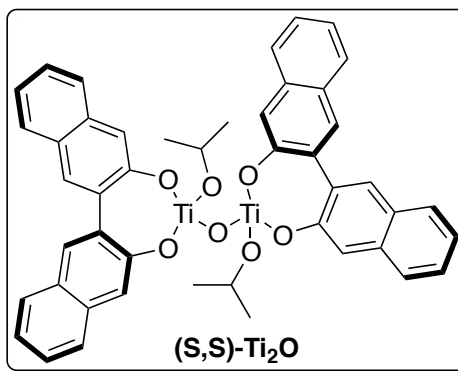
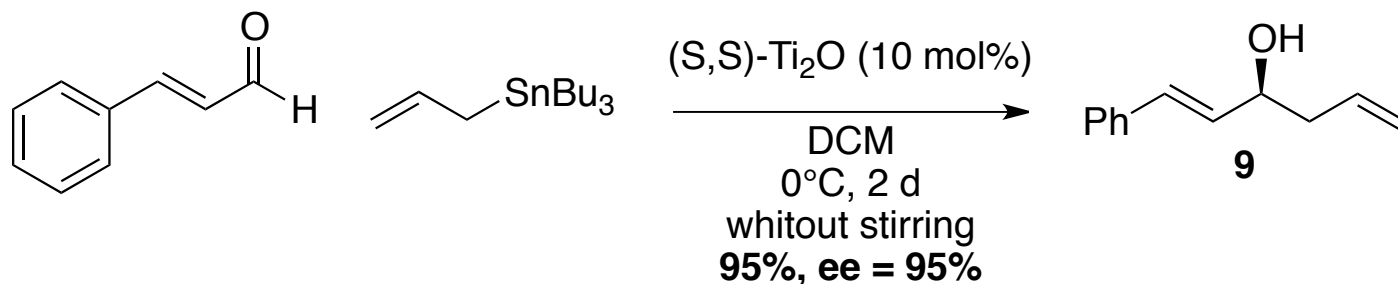
Plausible Mechanism for Silyl-directed Allylic Transposition/ Ring Contraction



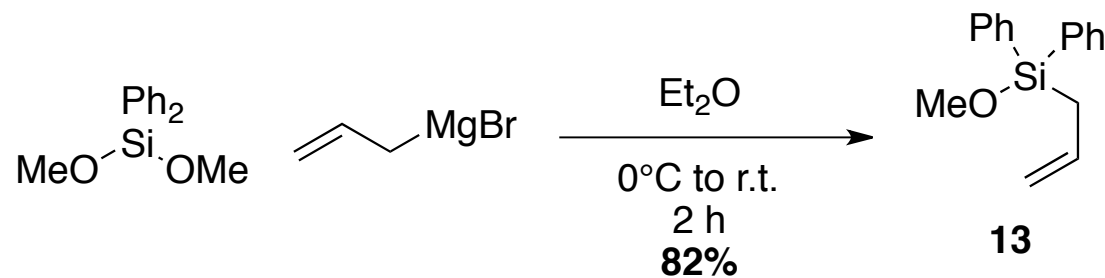
Synthesis of compound 10



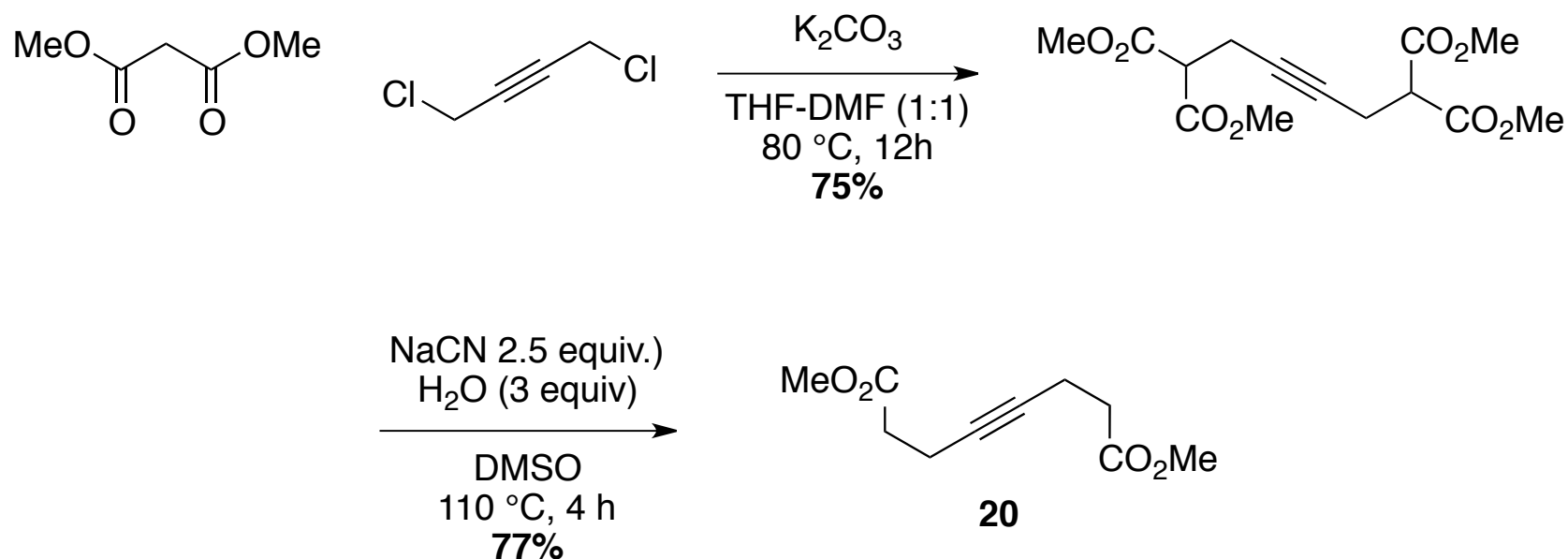
Synthesis of compound 9



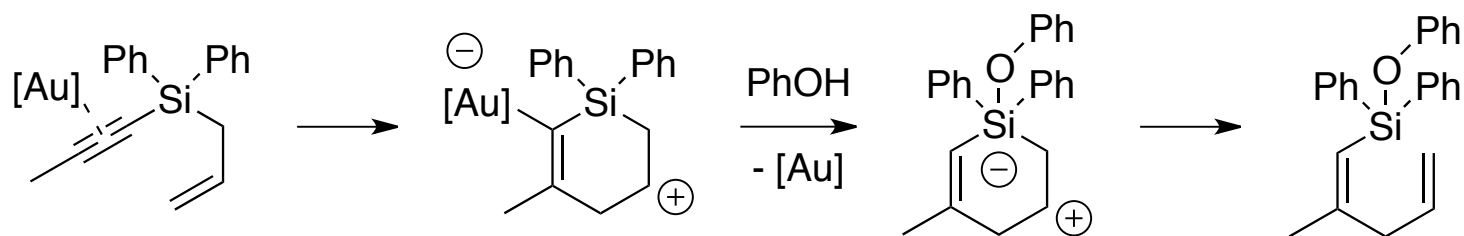
Synthesis of compound 13



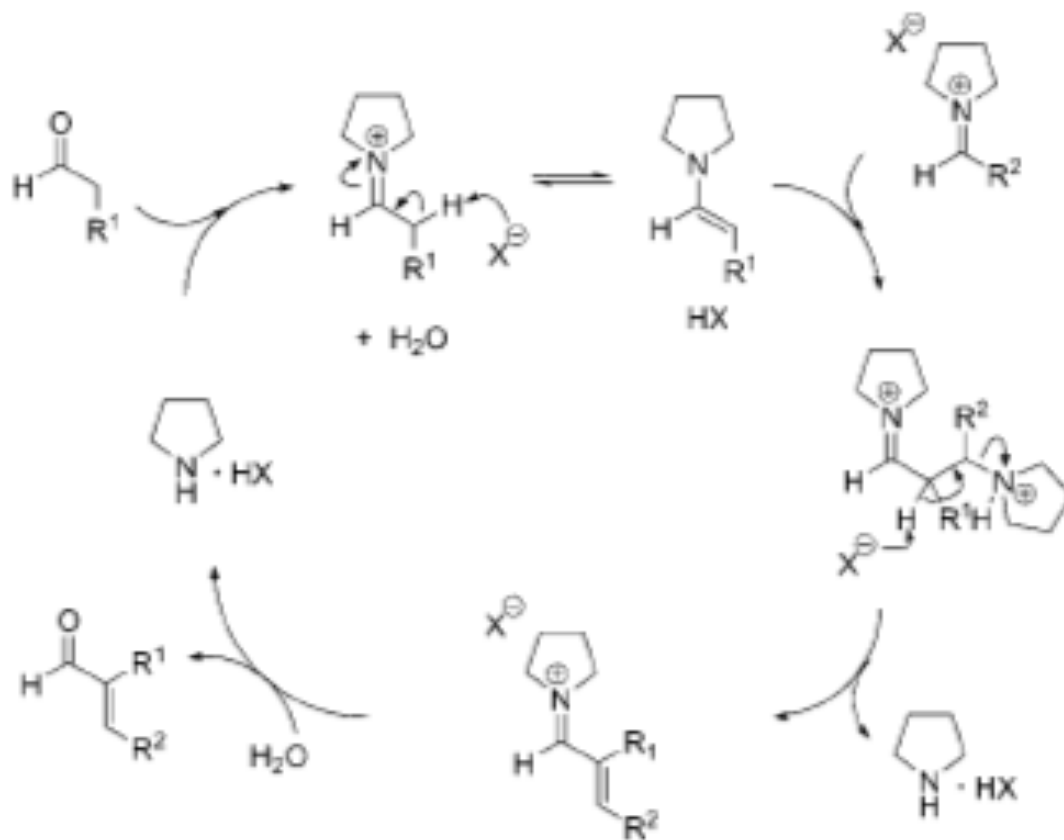
Synthesis of compound 20

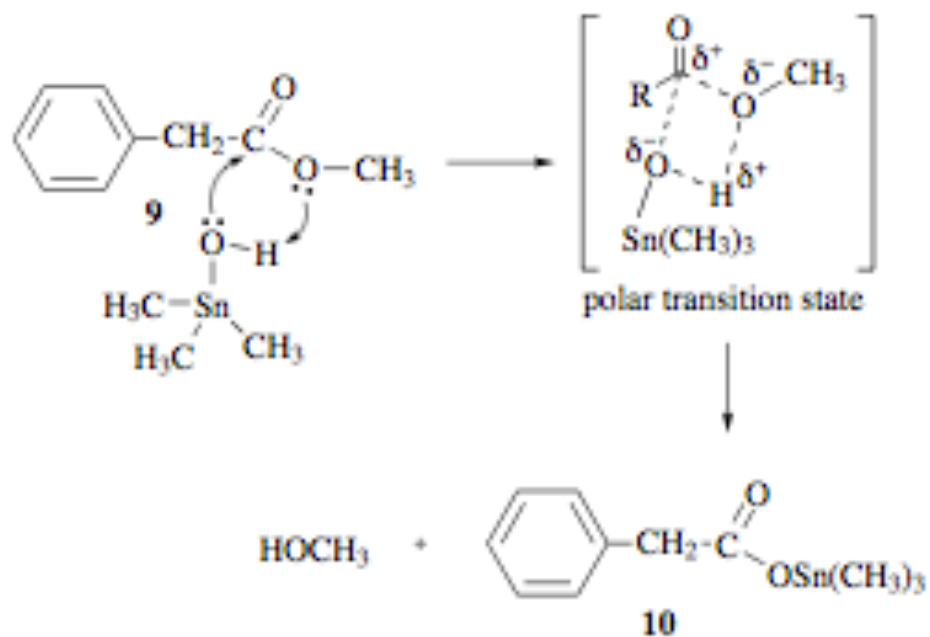


Gold-Catalyzed

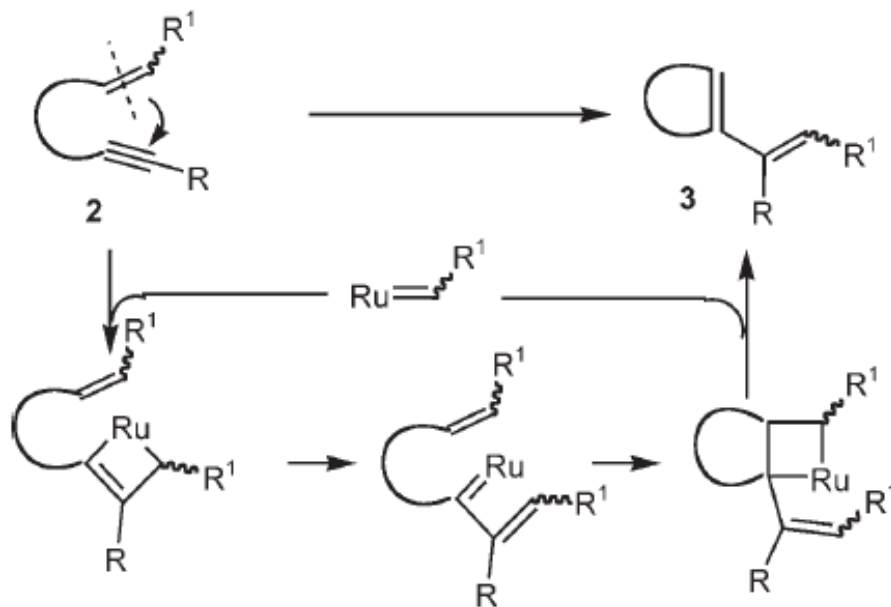


Knoevenagel-Mannich Type mechanism

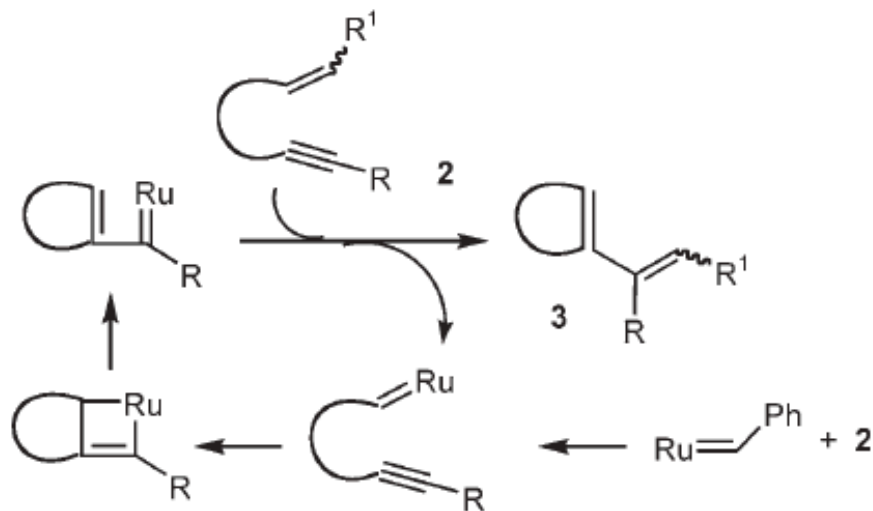




Route 1



Route 2



Retrosynthesis

