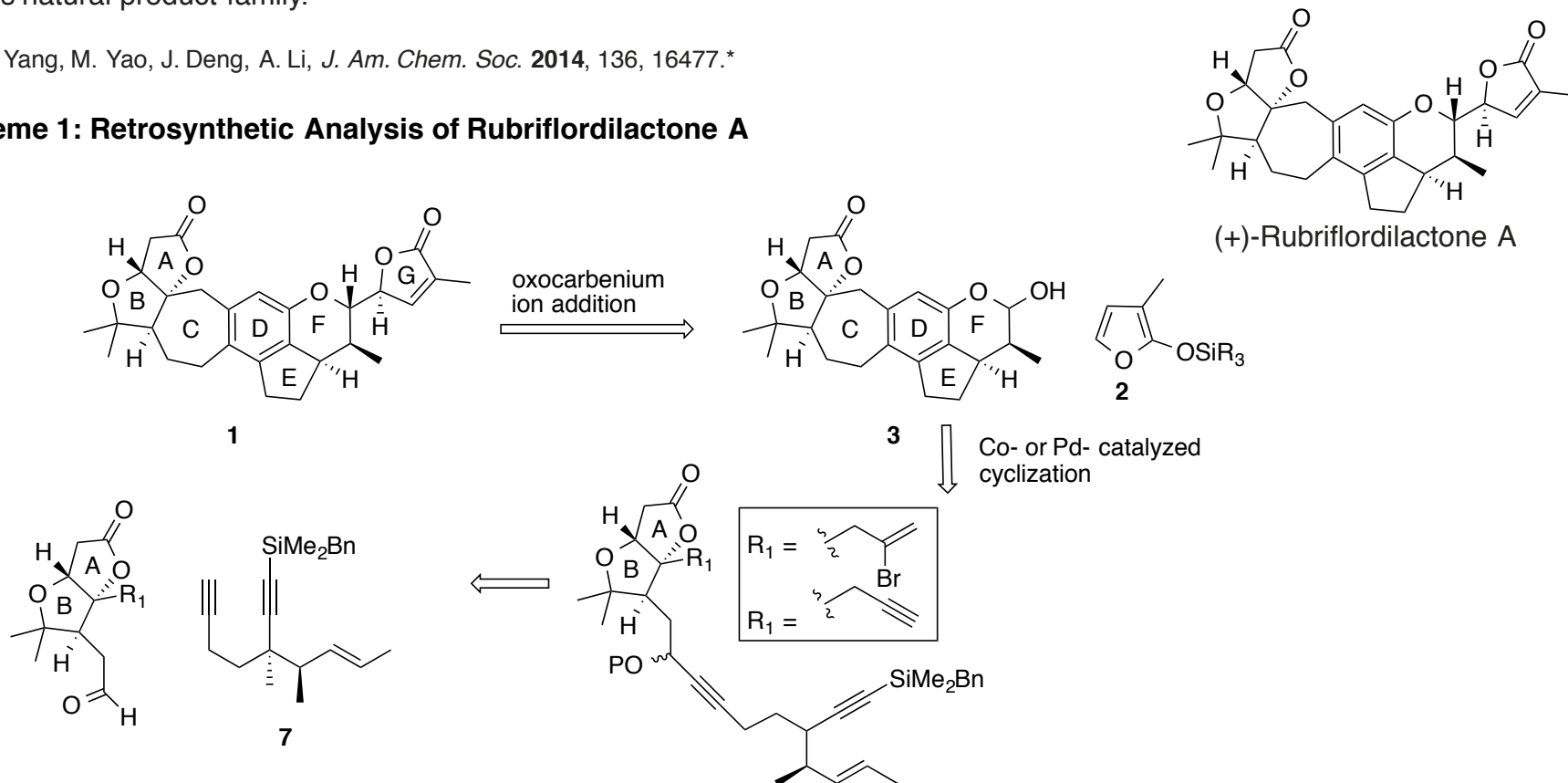


Introduction

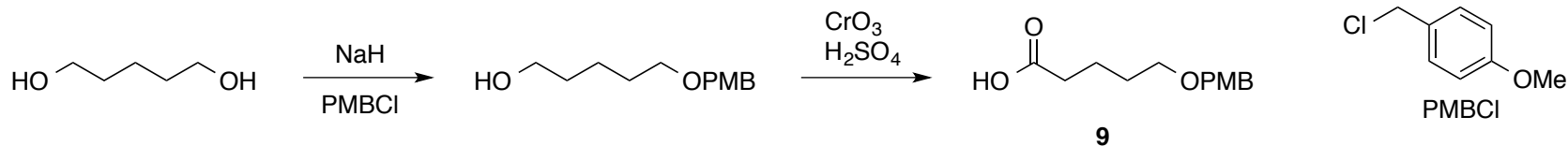
(+)-Rubriflordilactone A and its related family of nortriterpenoid natural products have been isolated from Chinese herbal plants such as *Schisandra* and *Kadsura* genera. Many of these natural products have demonstrated promising levels of anti-HIV activity. Rubriflordilactone A has been previously synthesized by Li and coworkers*. In this total synthesis, the authors employ either a Palladium or Cobalt catalyzed cyclization to construct the CDE rings (**Scheme 1**). The key cyclization step is set up by coupling a common diyne with two different AB ring aldehydes, a strategy that could be employed to synthesize other members of this natural product family.

Li, P. Yang, M. Yao, J. Deng, A. Li, *J. Am. Chem. Soc.* **2014**, 136, 16477.*

Scheme 1: Retrosynthetic Analysis of Rubriflordilactone A

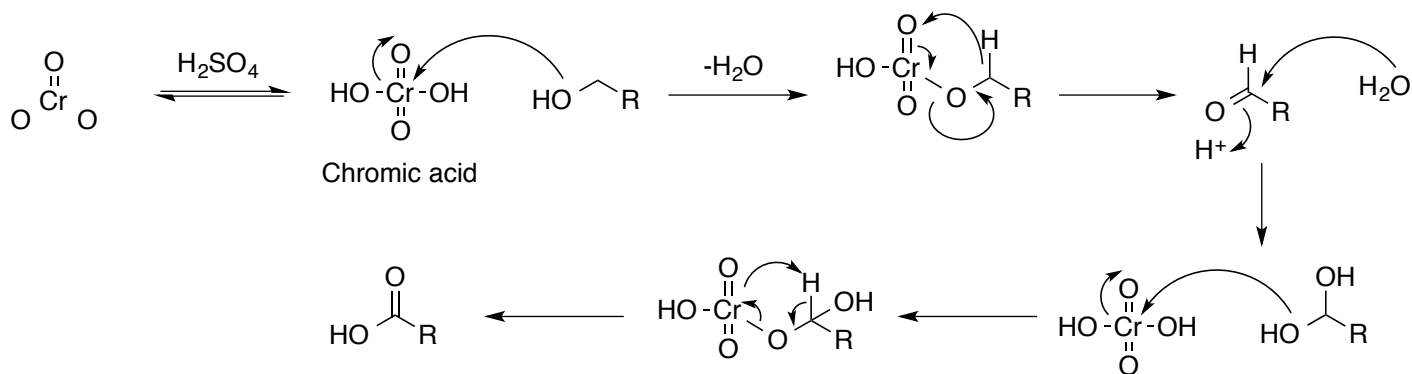


Scheme 2: Preparation of acid 9

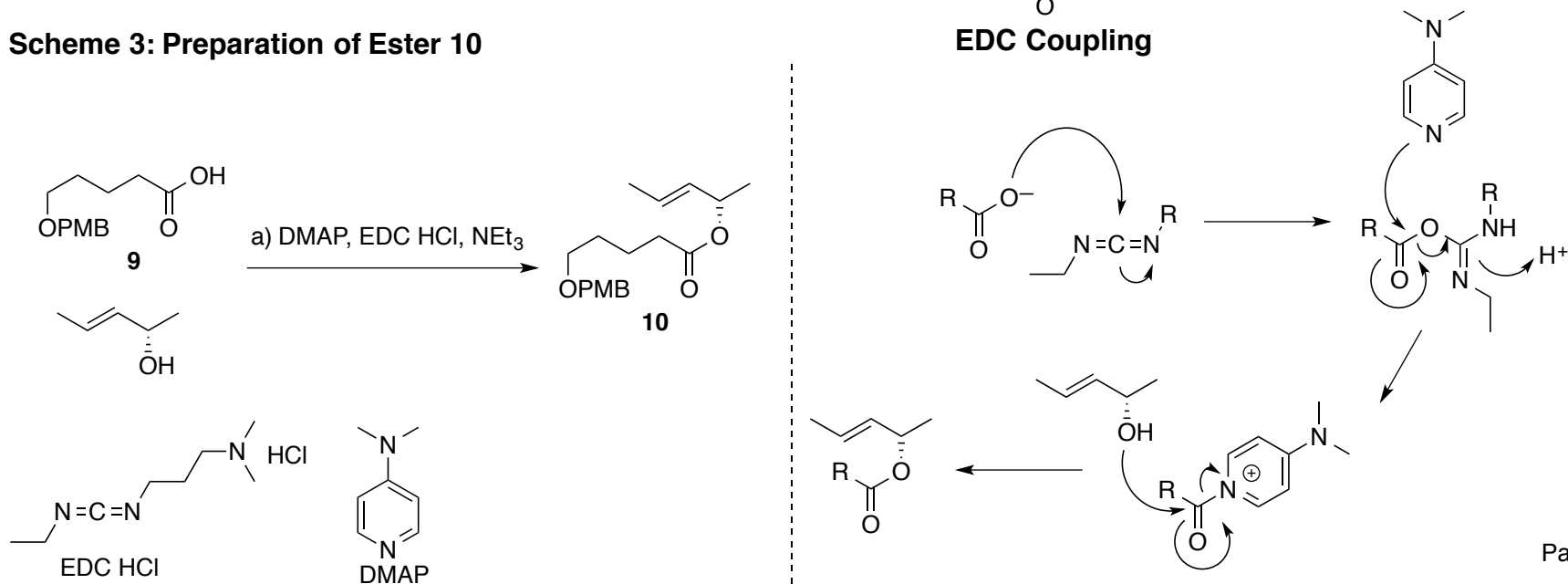


M. S. Wilson, J. C. S. Woo, G. R. Dake, *J. Org. Chem.* **2006**, 71, 4237.

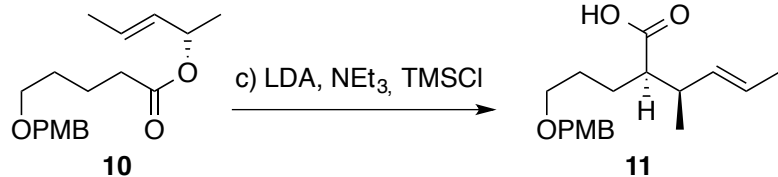
Jones Oxidation



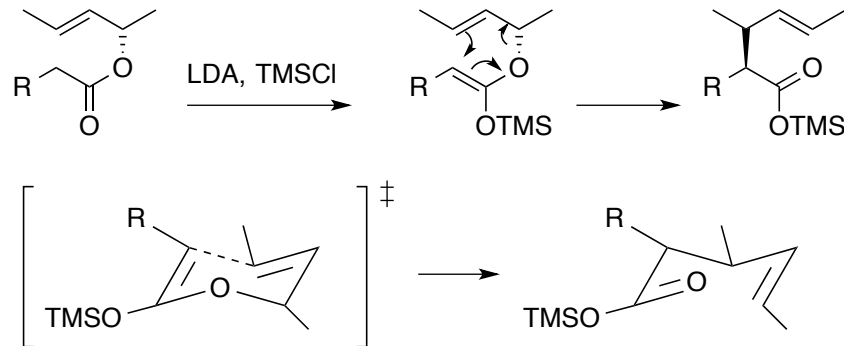
Scheme 3: Preparation of Ester 10



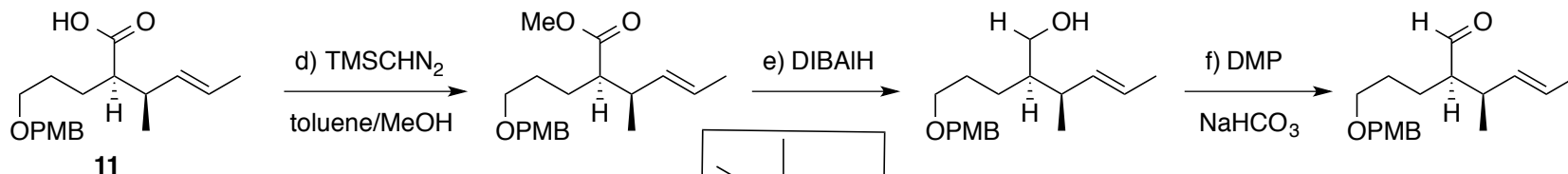
Scheme 4: Ireland-Claisen Rearrangement



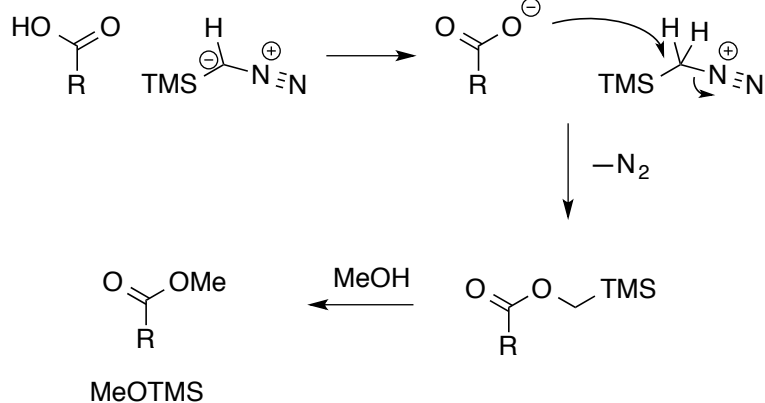
Ireland-Claisen Rearrangement



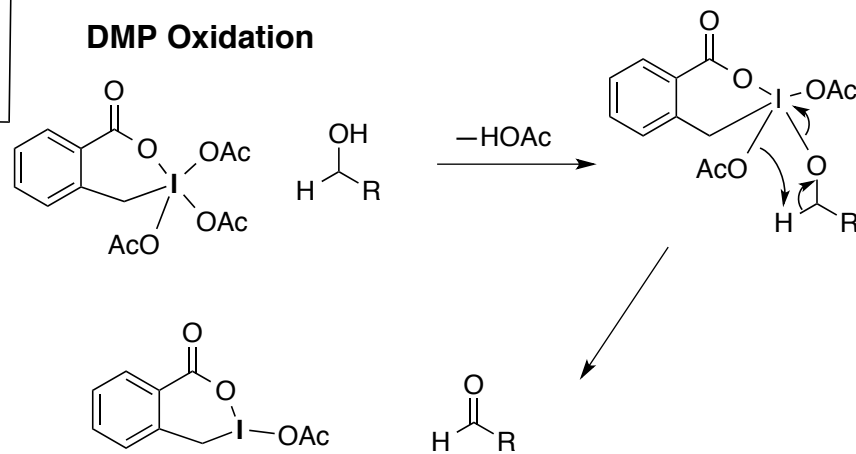
Scheme 5: Conversion of Acid to Aldehyde



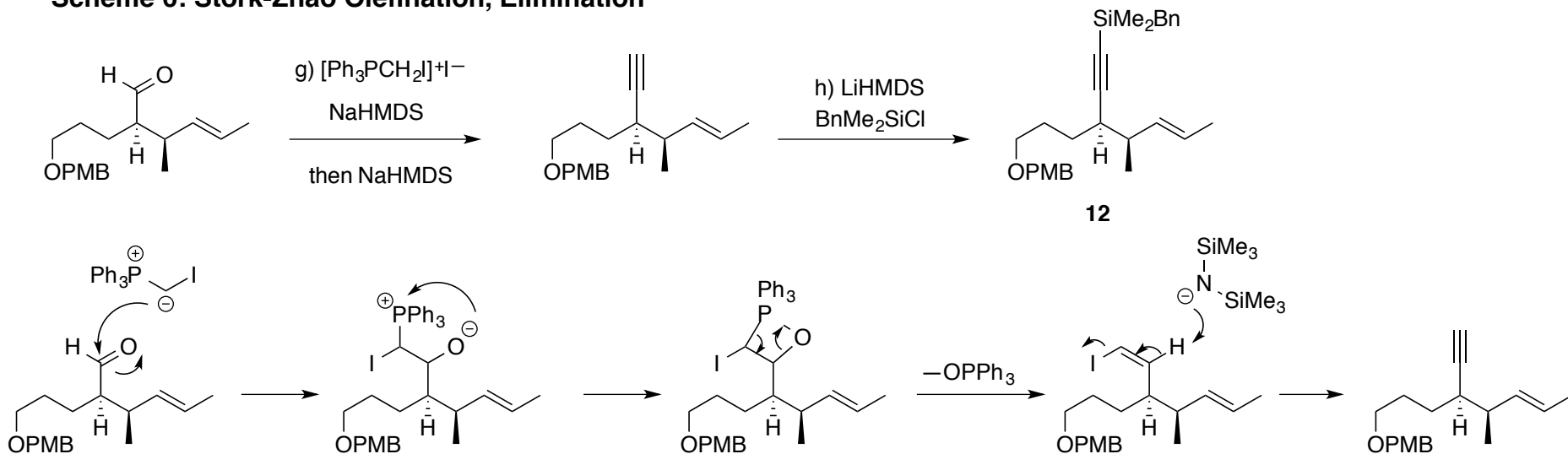
Esterification



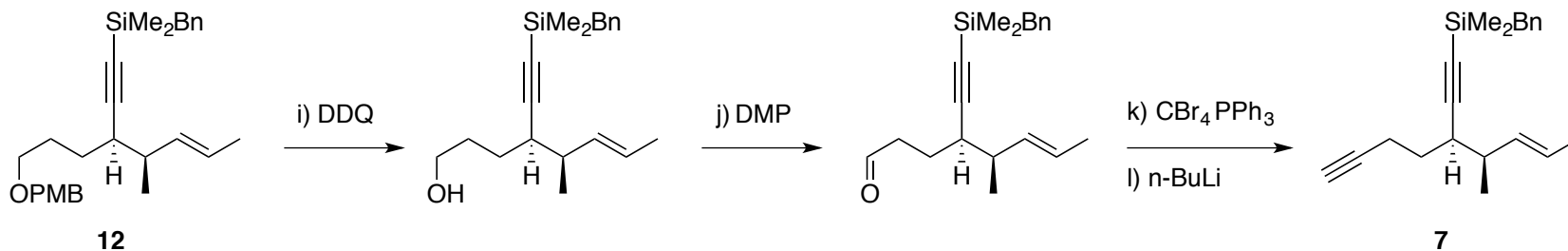
DMP Oxidation



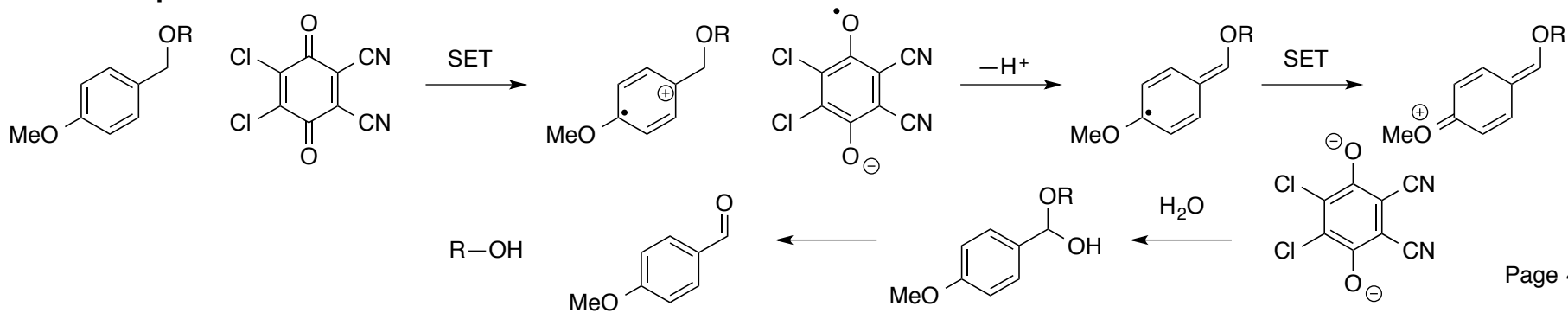
Scheme 6: Stork-Zhao Olefination, Elimination



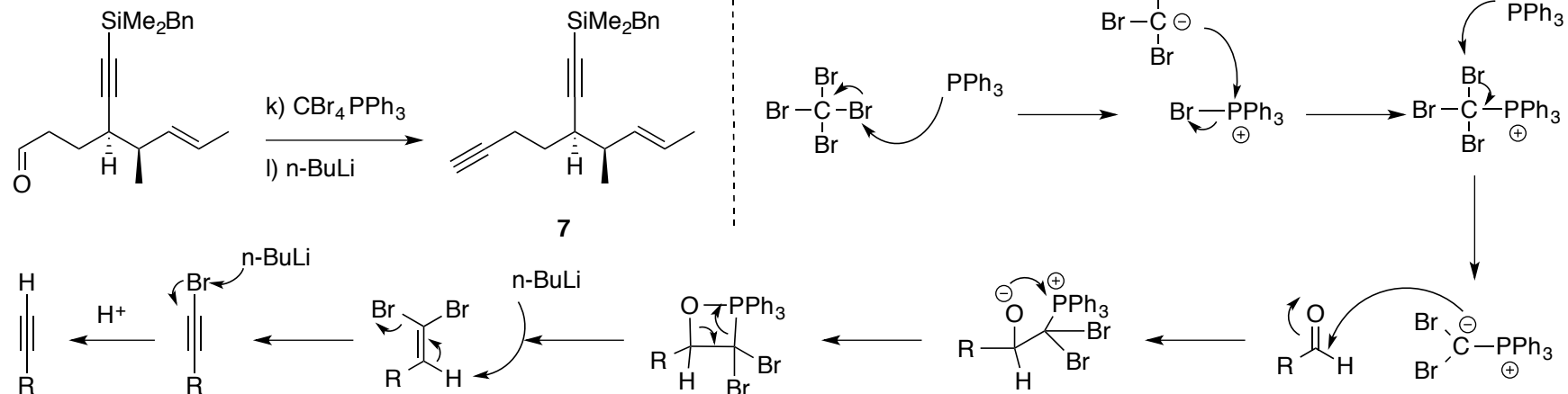
Scheme 7: Corey-Fuchs Homologation



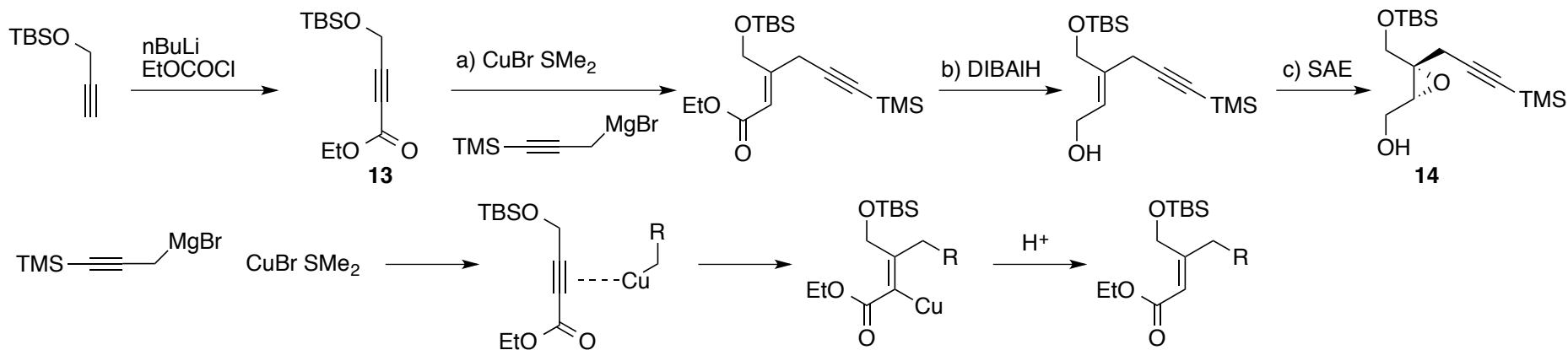
DDQ Deprotection



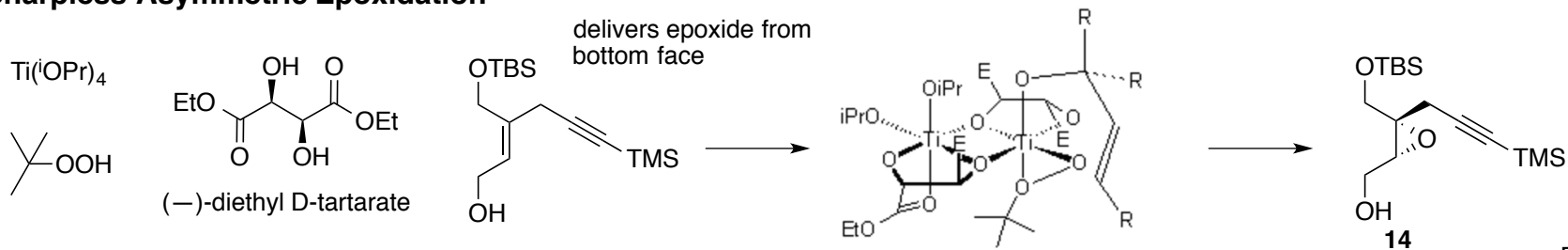
Corey-Fuchs Homologation



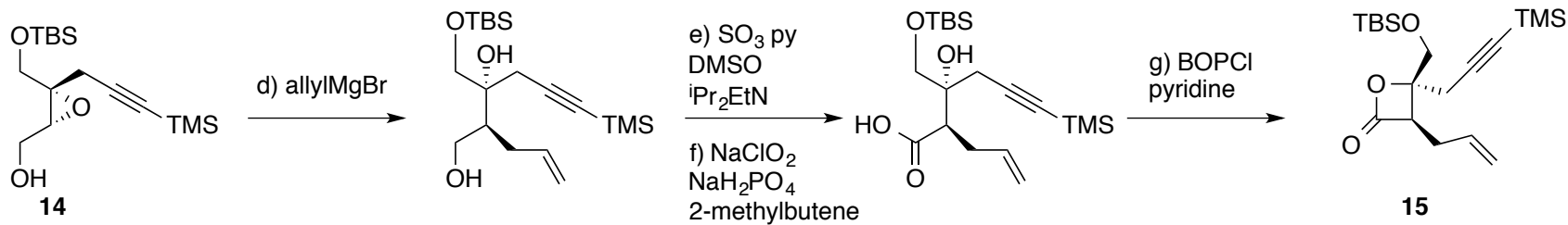
Scheme 8: Preparation of Epoxide **14**



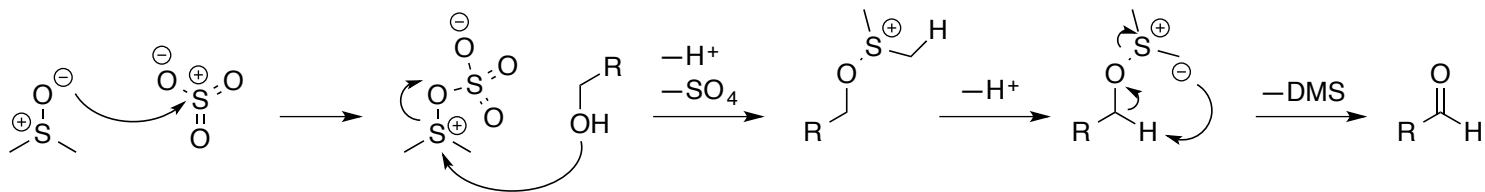
Sharpless Asymmetric Epoxidation



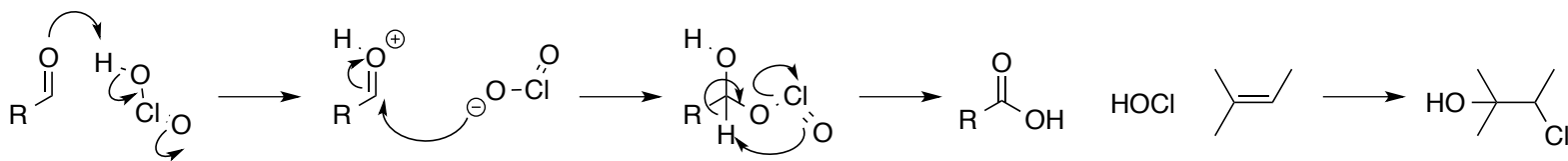
Scheme 9: Preparation of beta-lactone 15



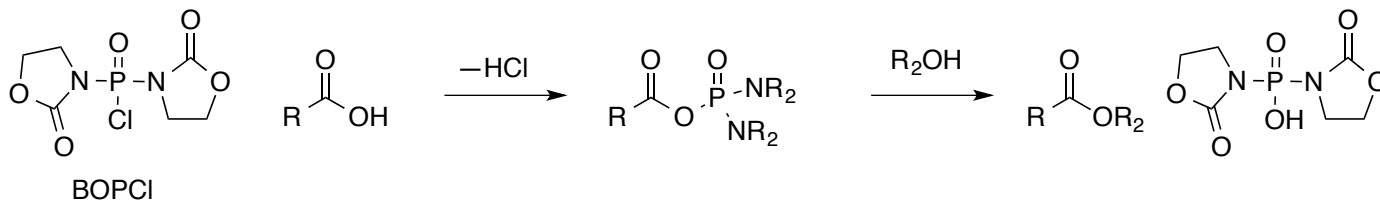
Parikh-Doering Oxidation



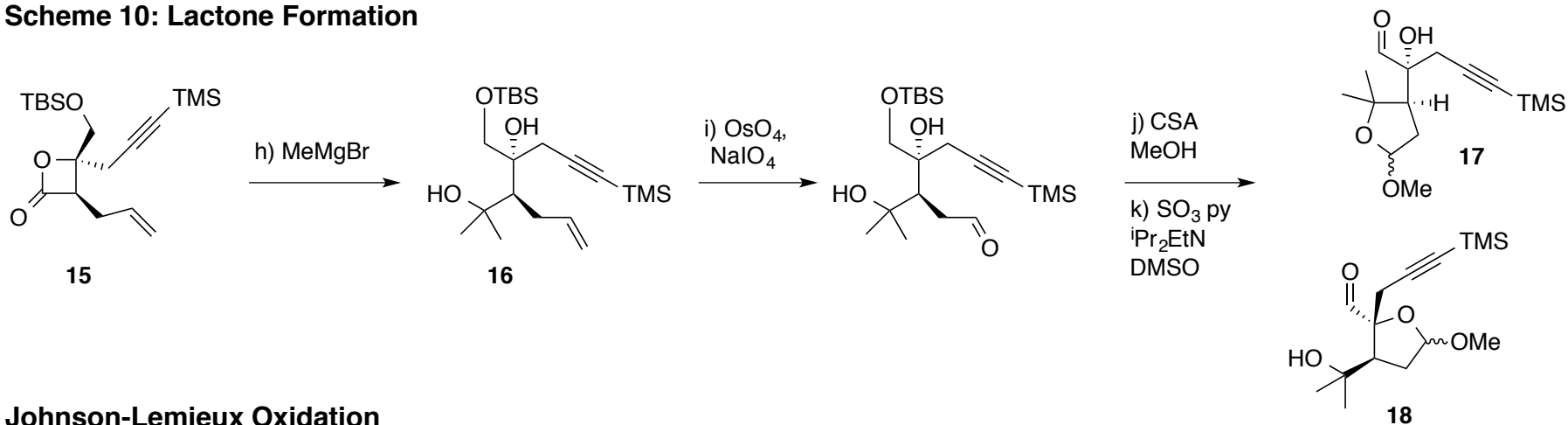
Pinnick Oxidation



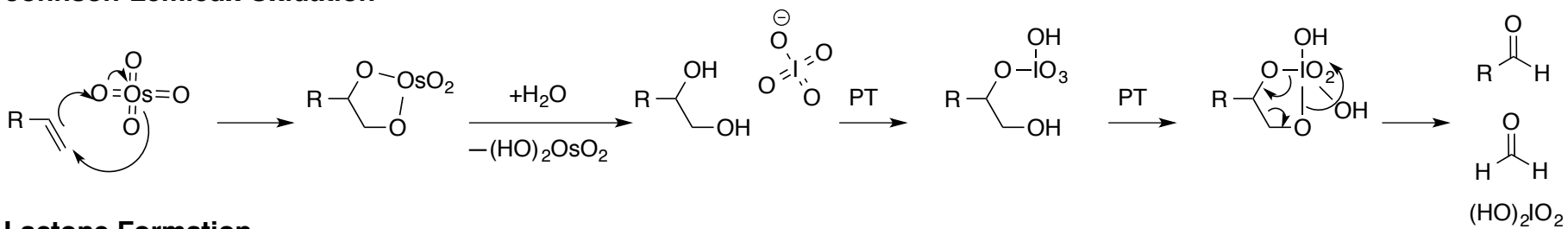
Lactone Formation



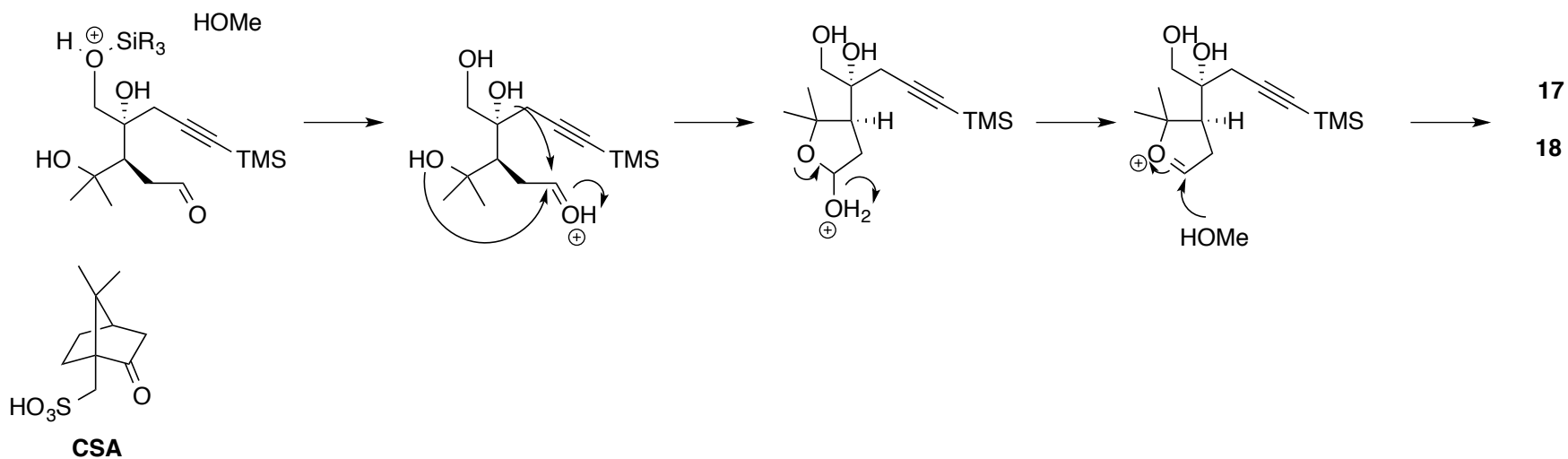
Scheme 10: Lactone Formation



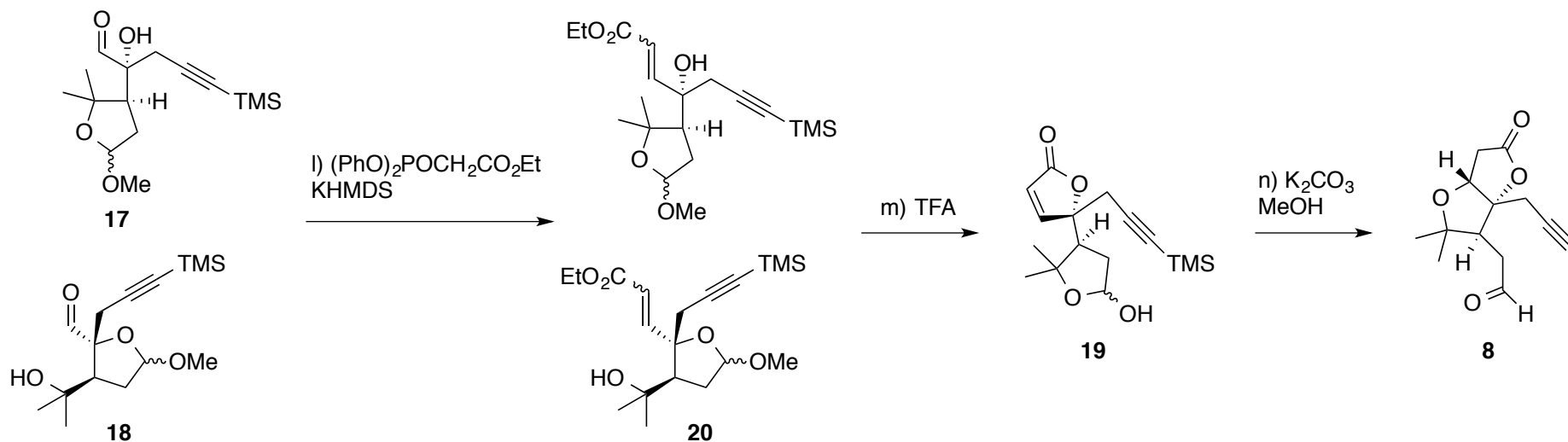
Johnson-Lemieux Oxidation



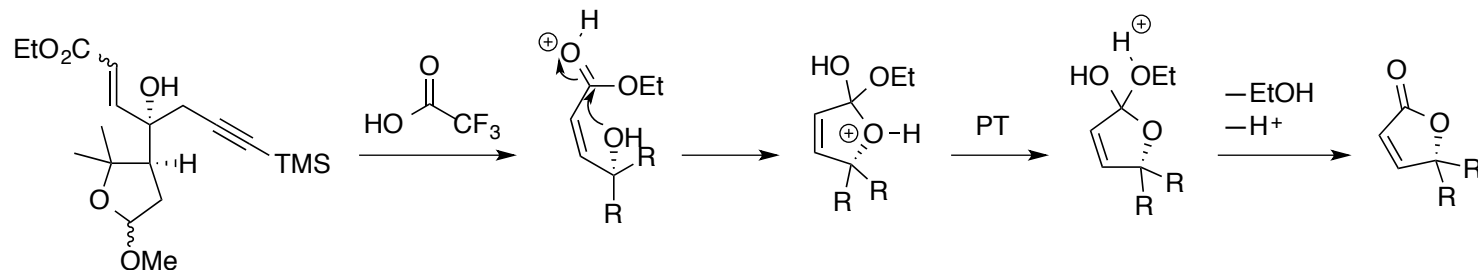
Lactone Formation



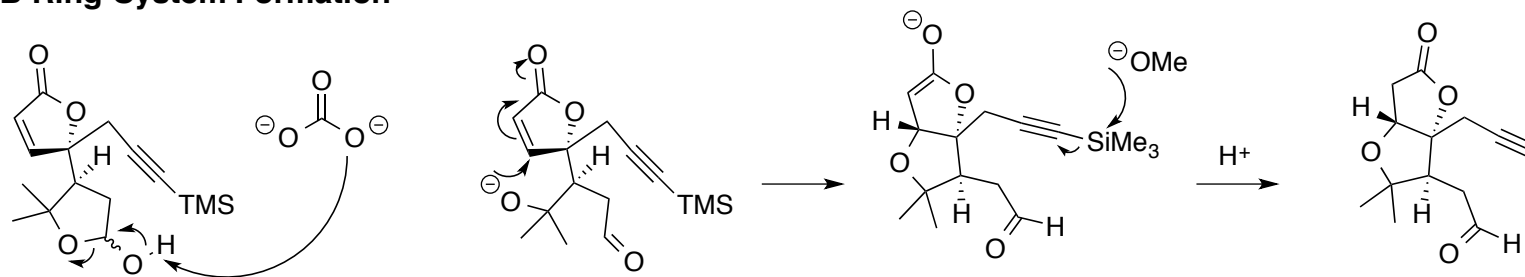
Scheme 11: Convergence of Lactones 17 and 18



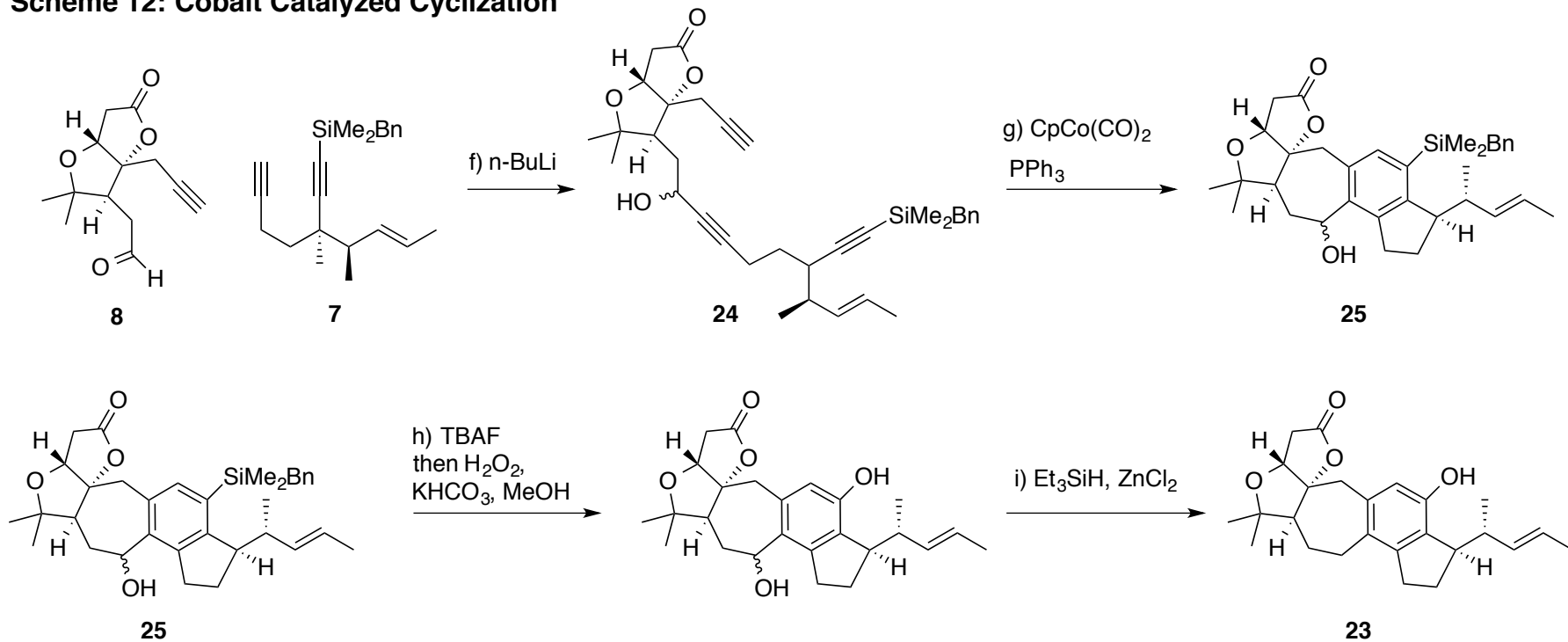
Alpha, Beta Unsaturated Lactone Formation



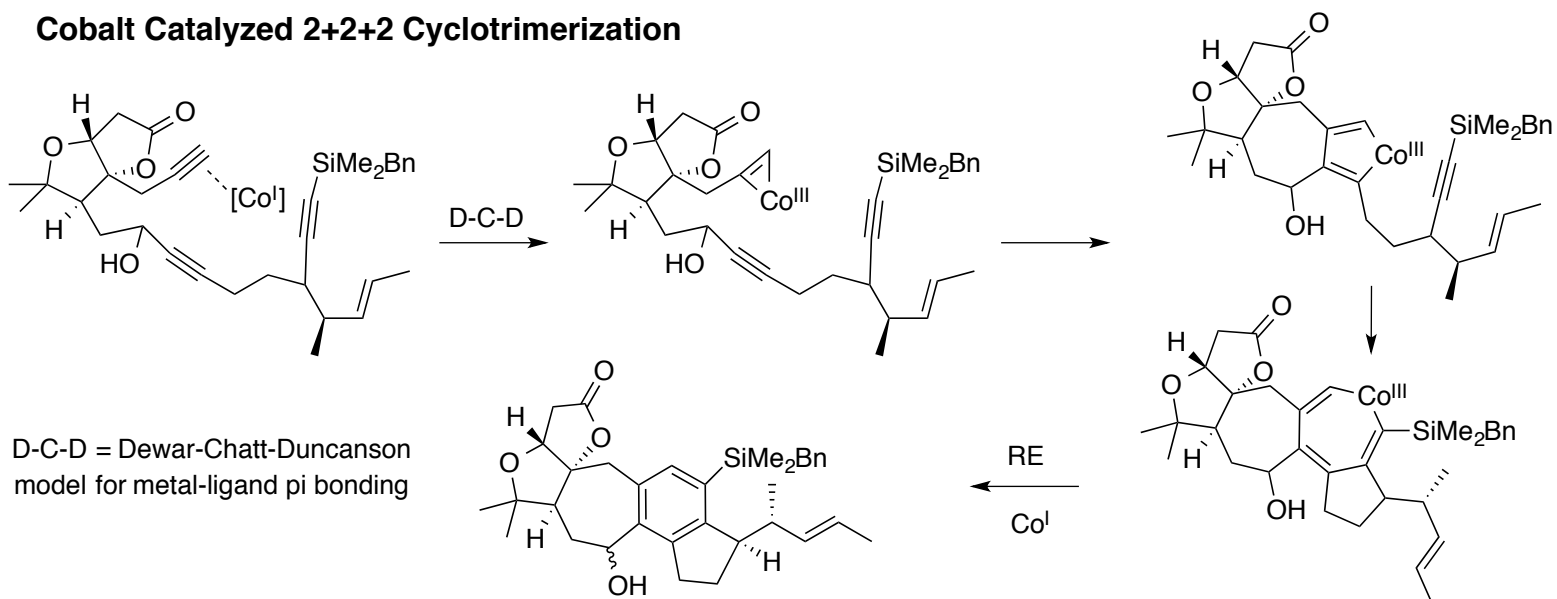
A B Ring System Formation



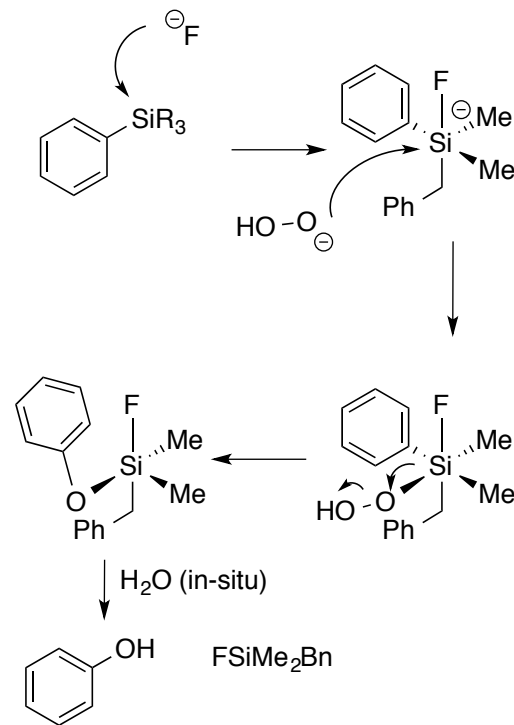
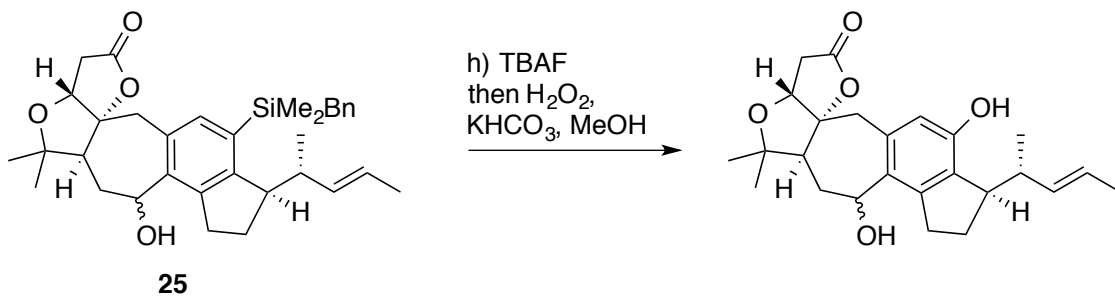
Scheme 12: Cobalt Catalyzed Cyclization



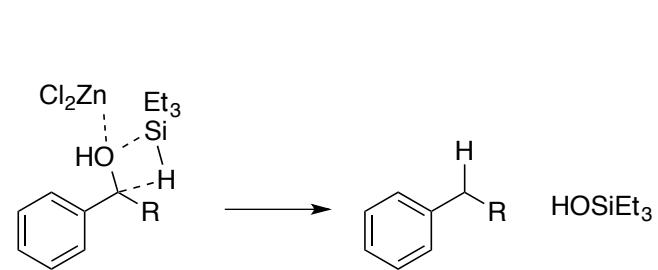
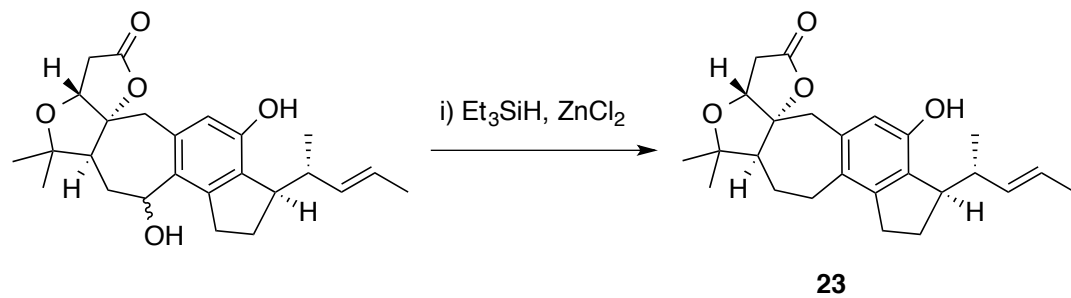
Cobalt Catalyzed 2+2+2 Cyclotrimerization



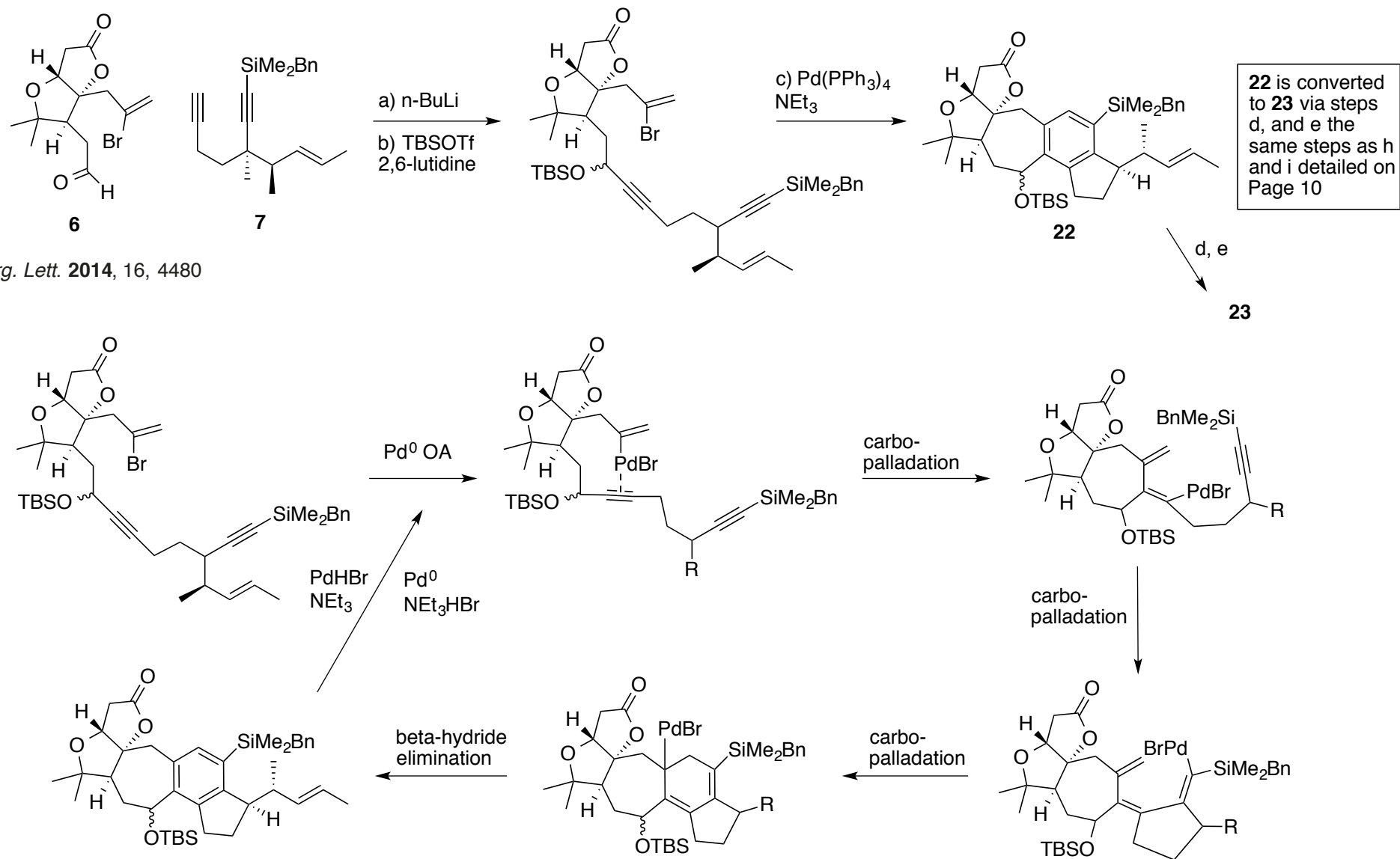
Tamao Oxidation



Benzylic Reduction

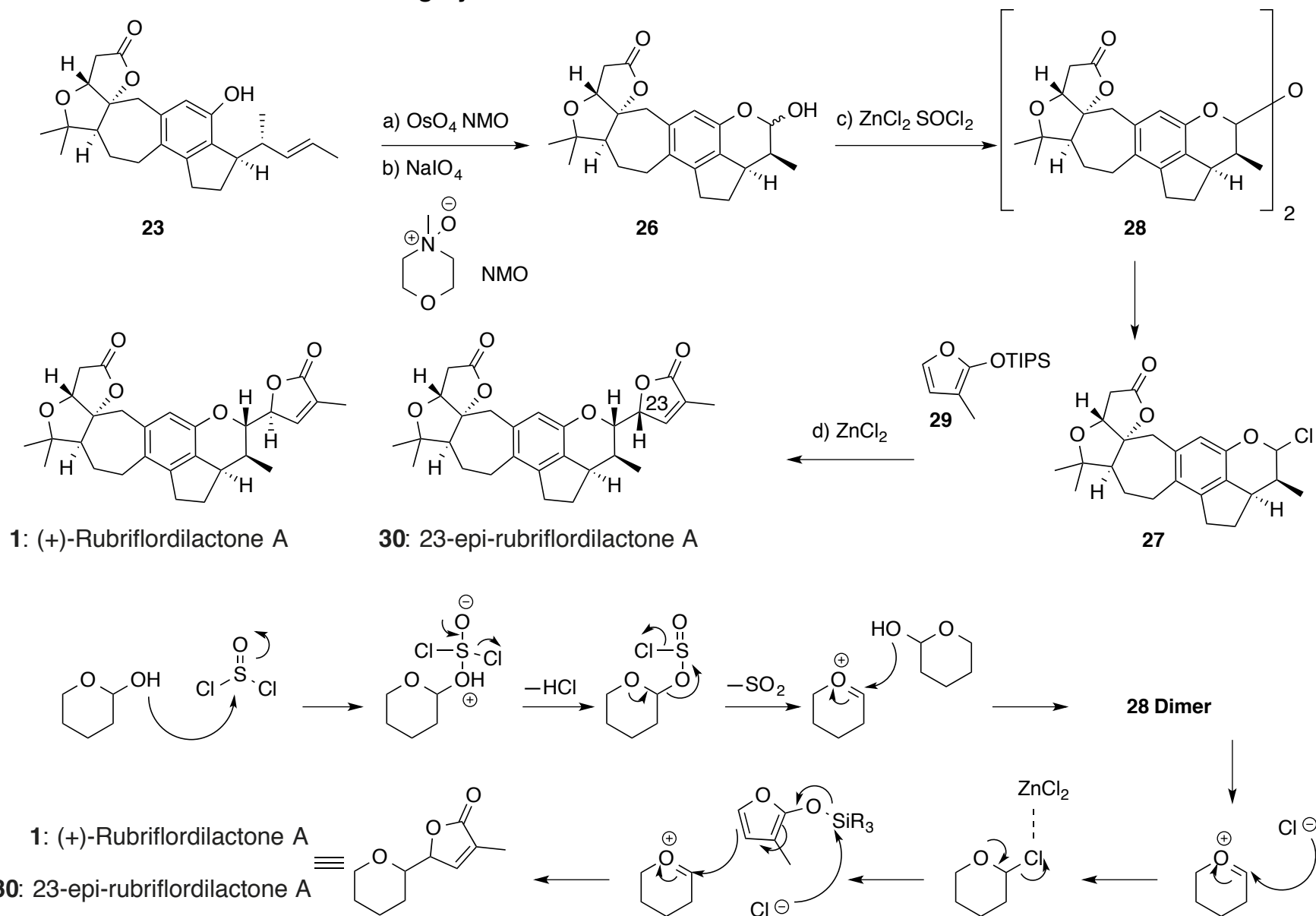


Scheme 13: Palladium Catalyzed Cyclization



Org. Lett. 2014, 16, 4480

Scheme 14: Elaboration of FG Ring System



Conclusion: synthesized final product in 37 total steps, 24 steps longest linear sequence.