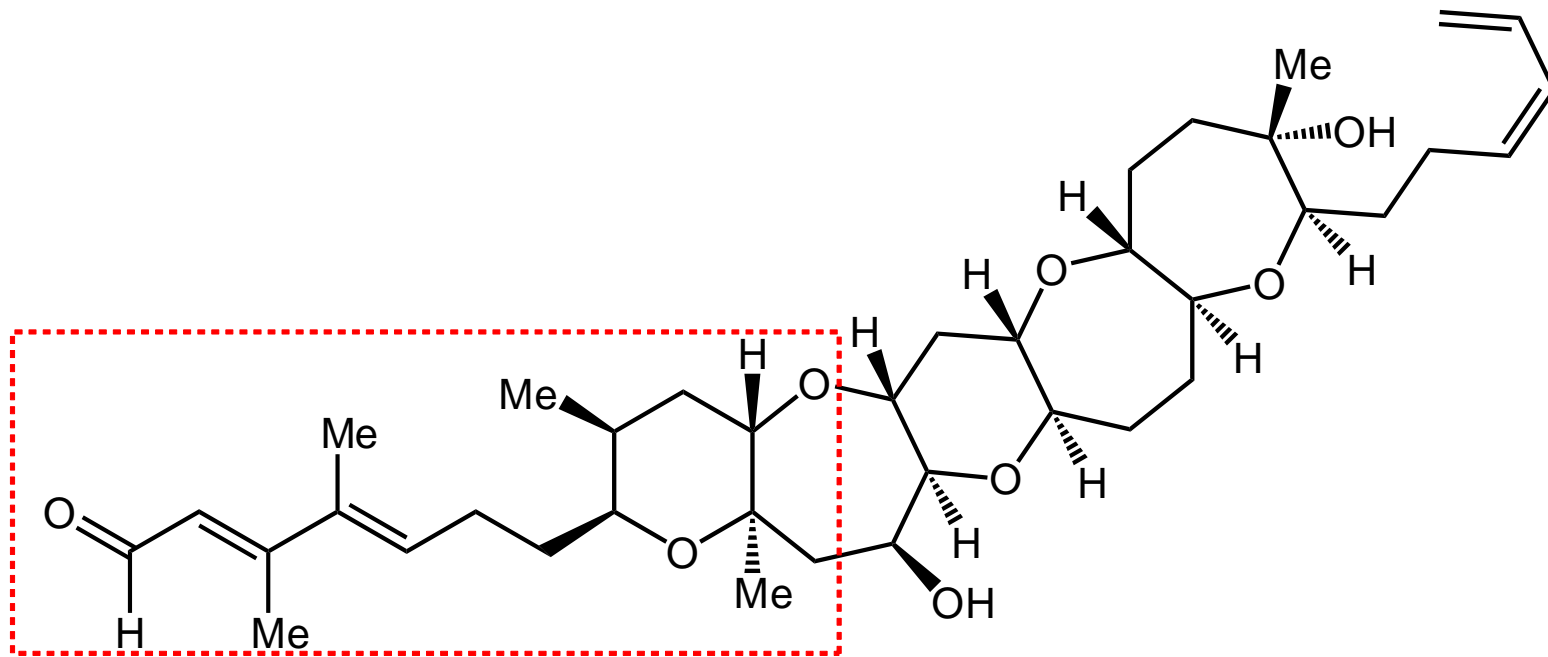


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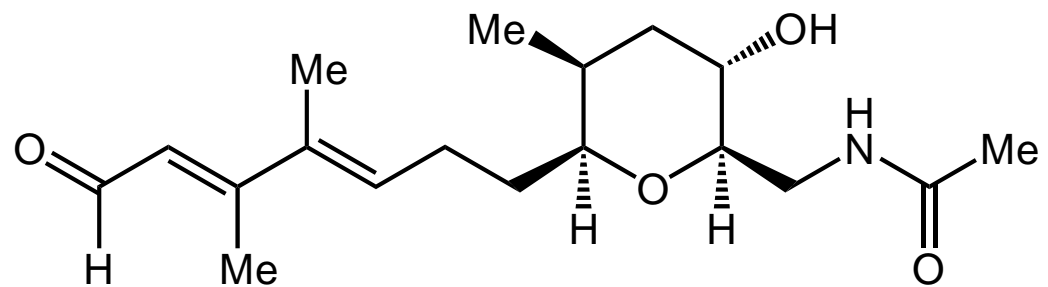
陈木旺 检查: 陈庆安

An Asymmetric Total Synthesis of Brevisamide

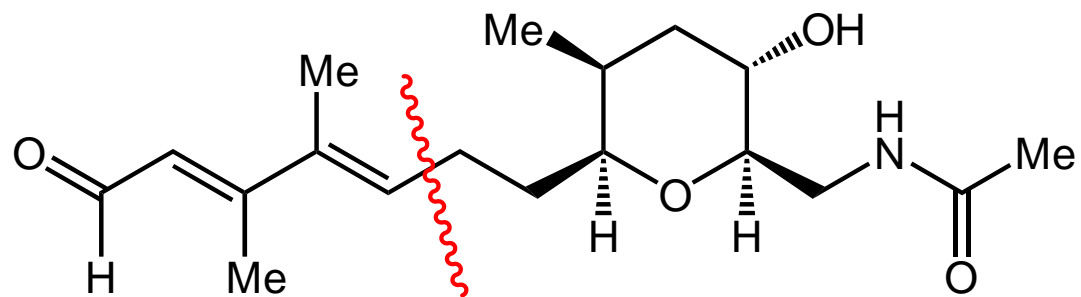
Ghosh, A. K.* *et al*
Org. Lett. **2009**, *11*, 4164-4167.



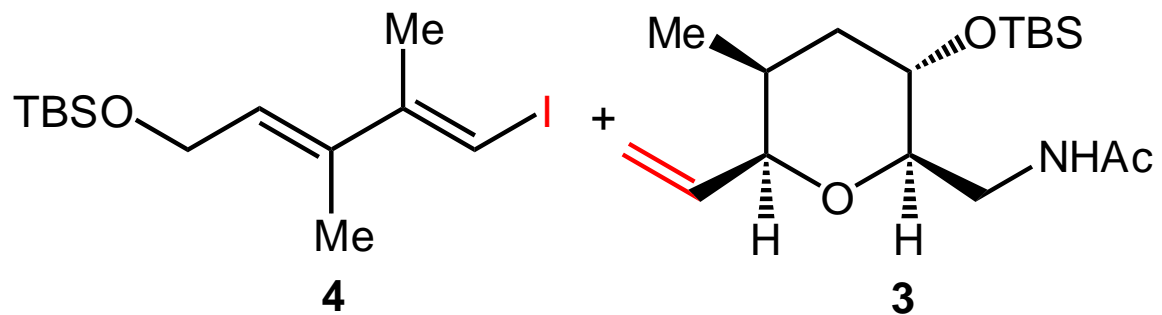
Brevenal (1)



Brevisamide (2)

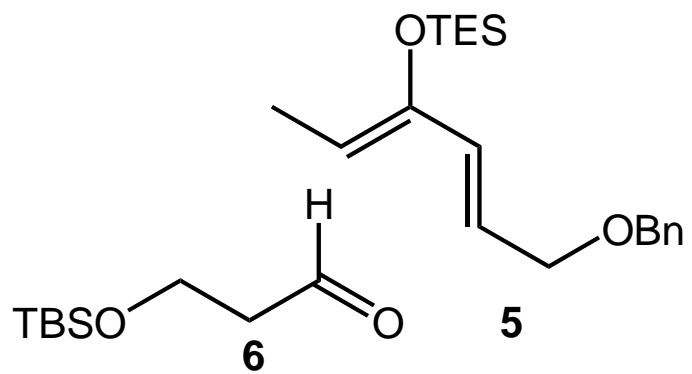
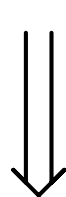
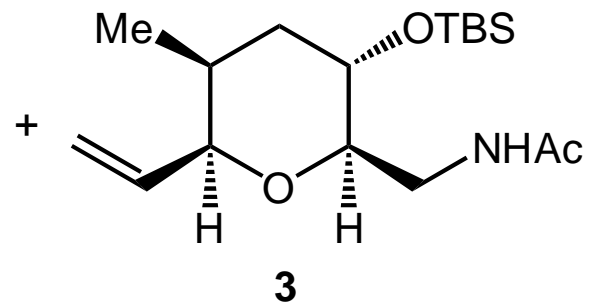
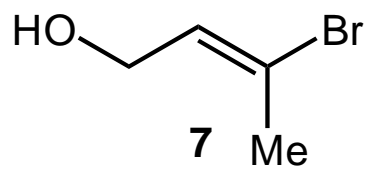
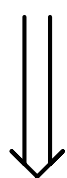
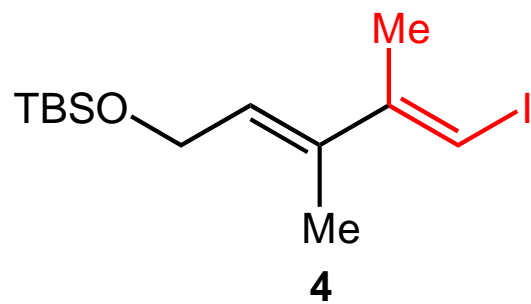


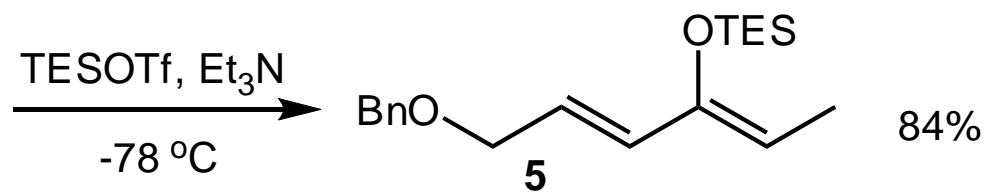
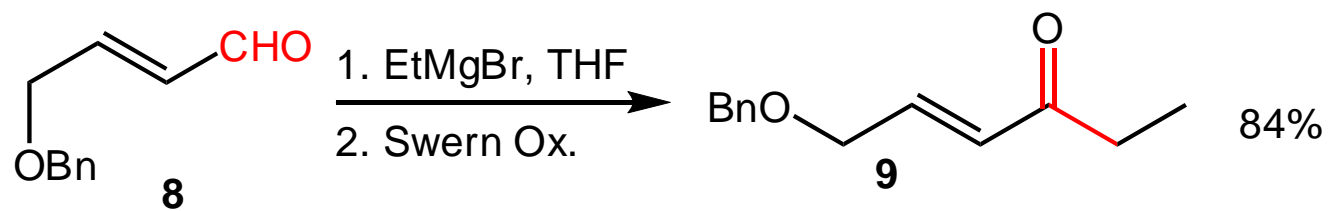
2

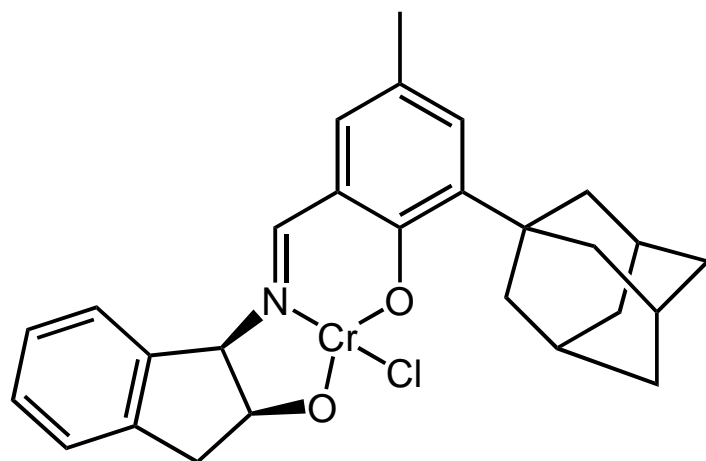
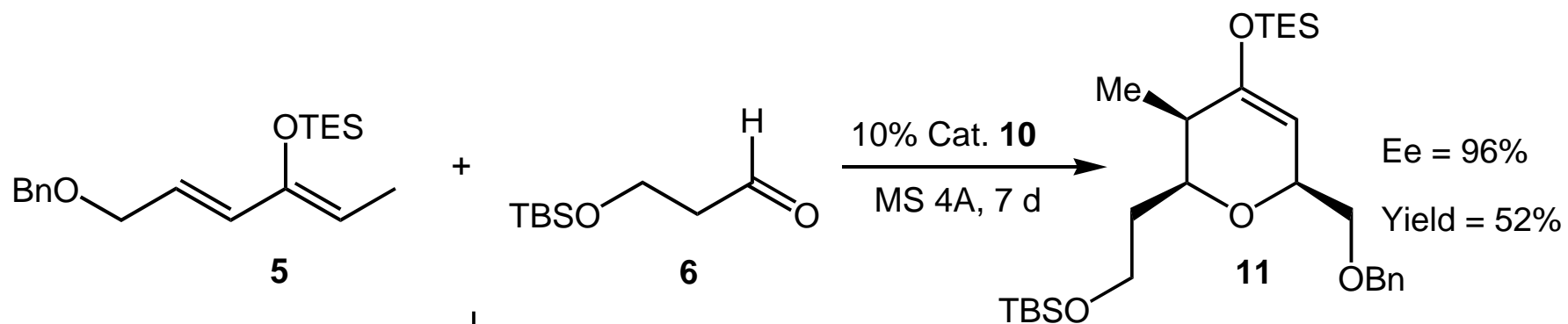


4

3

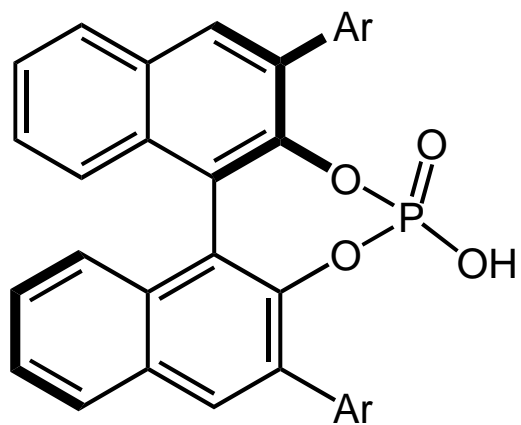
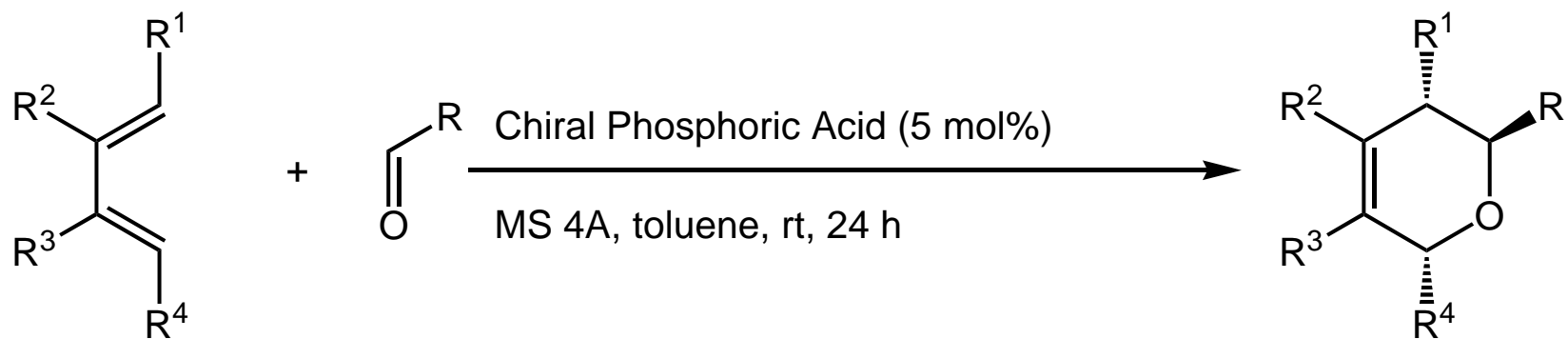






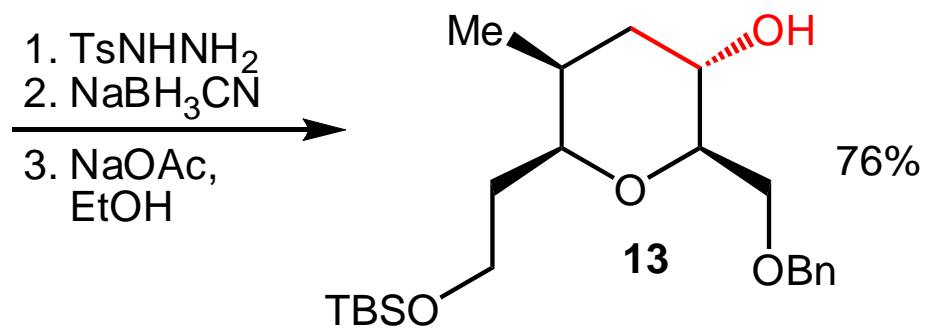
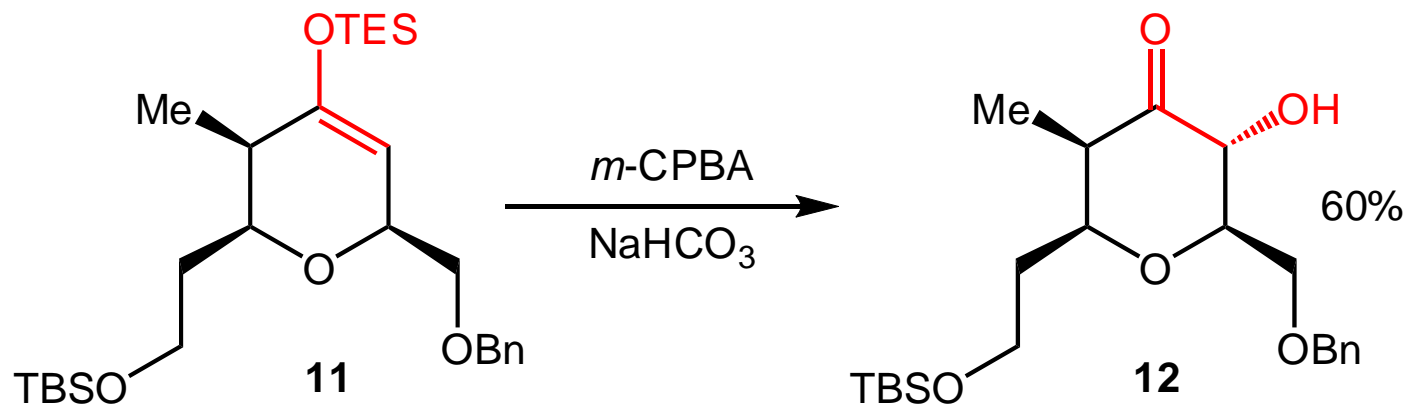
Jacobsen's chromium catalyst **10**

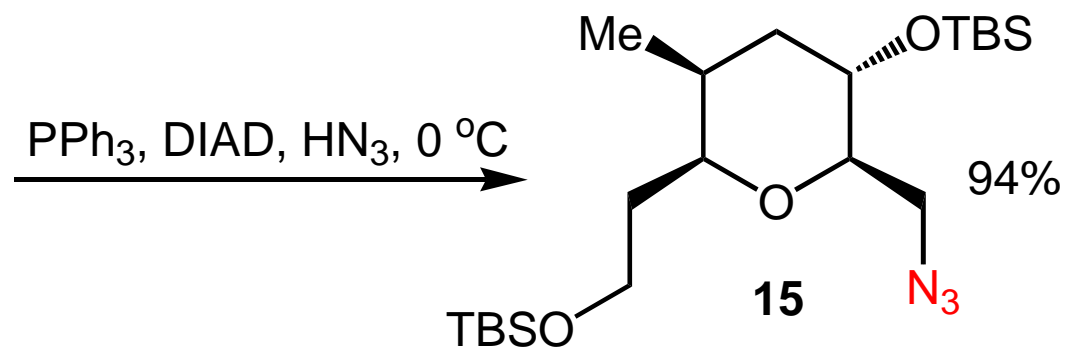
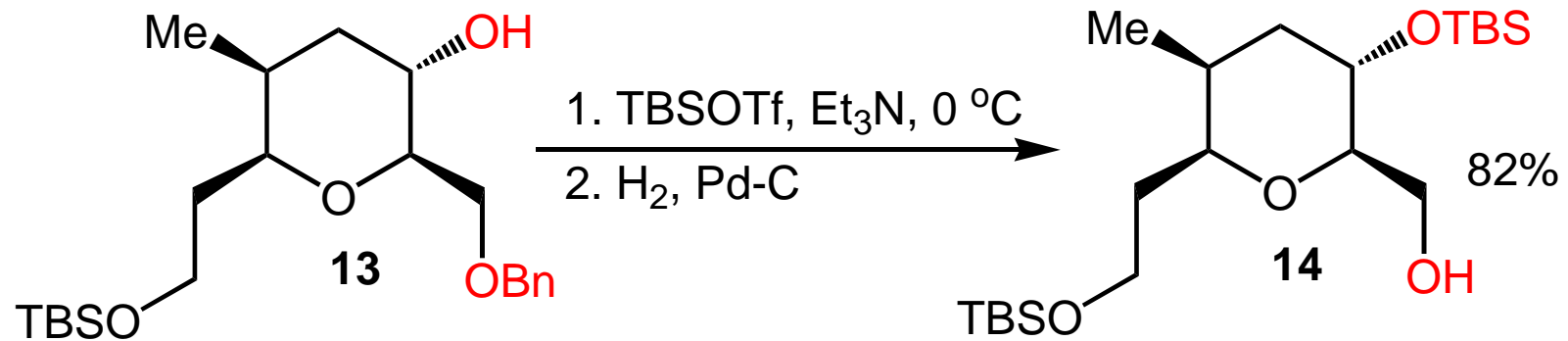
Dossetter, A. G.; Jamison, T. F.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **1999**, *38*, 2398-2400.

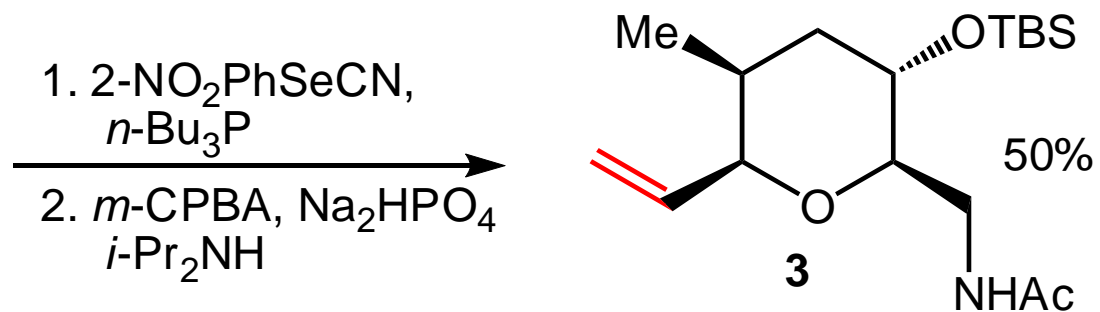
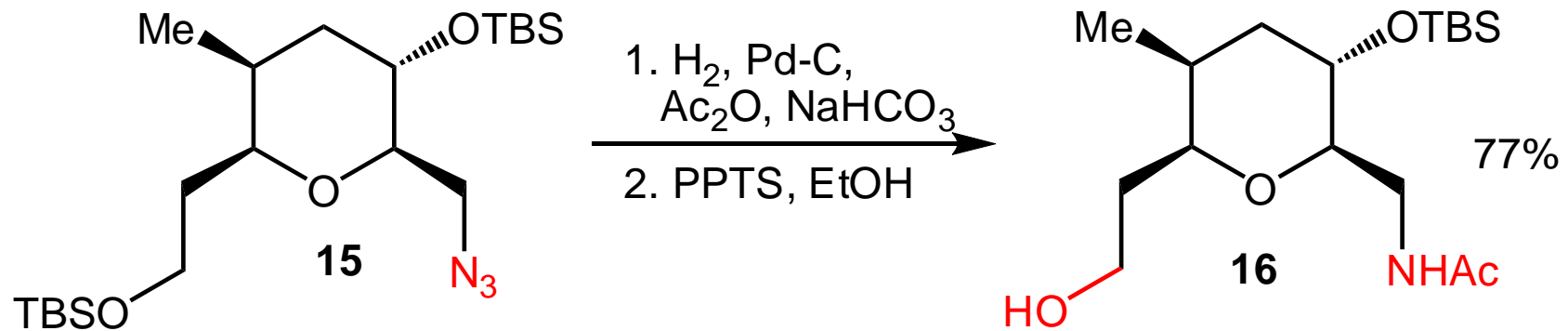


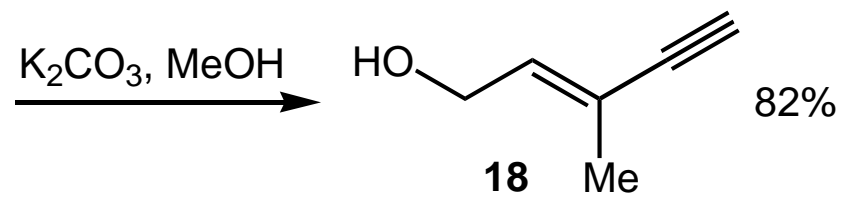
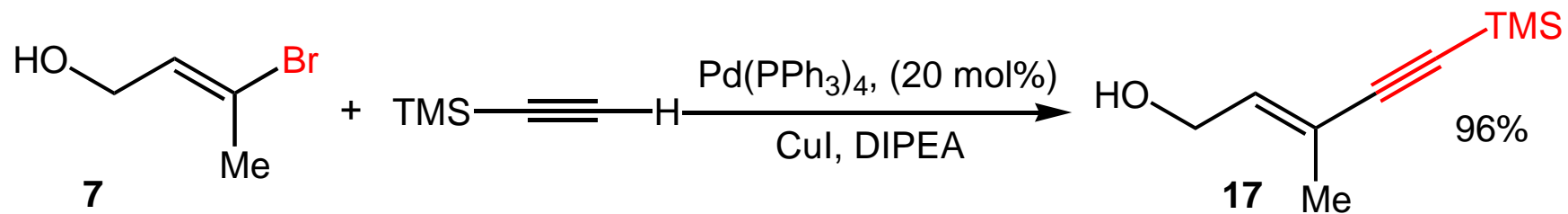
- 1a:** Ar = Ph
1b: Ar = (3, 5-Ph₂)C₆H₃-
1c: Ar = (2, 4, 6-^{*i*}Pr₃)C₆H₂-

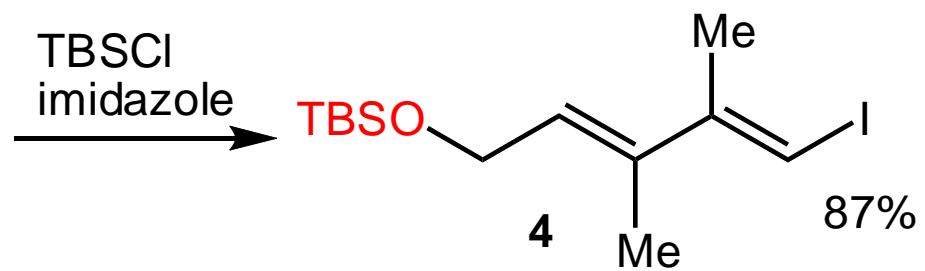
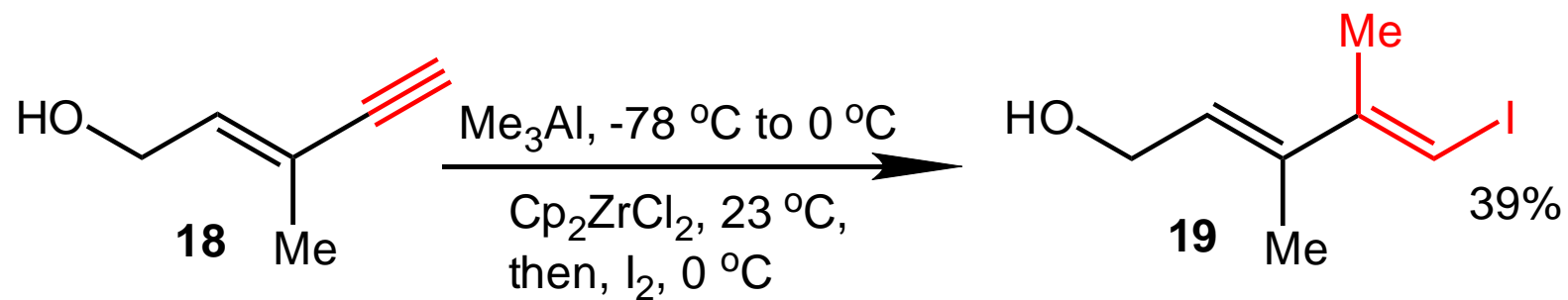
Momiyama, N.; Tabuse, H.; Terada, M. *J. Am. Chem. Soc.* **2009**, *131*, 12882–12883.

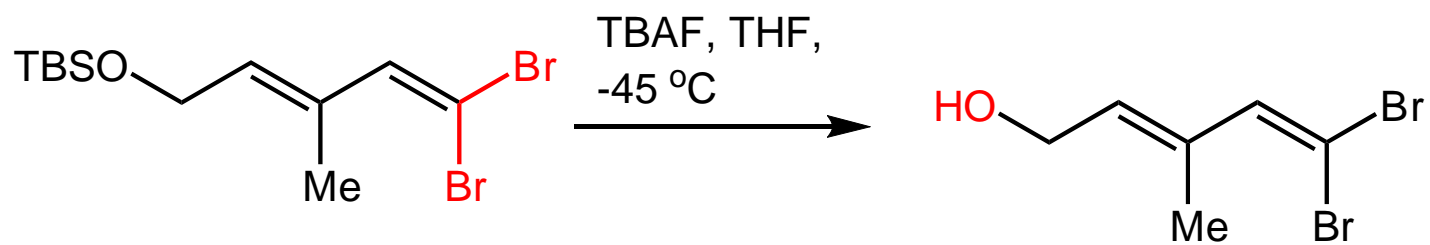
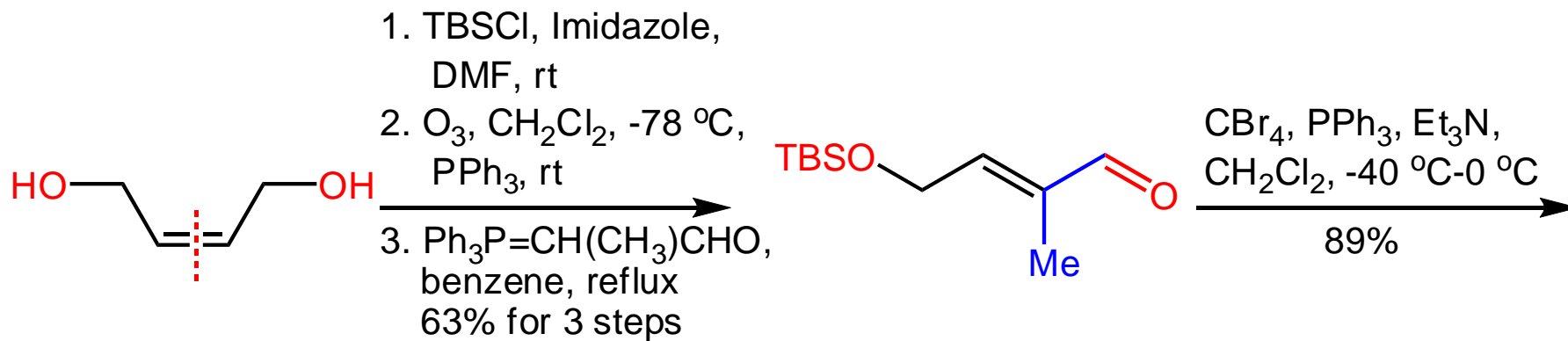




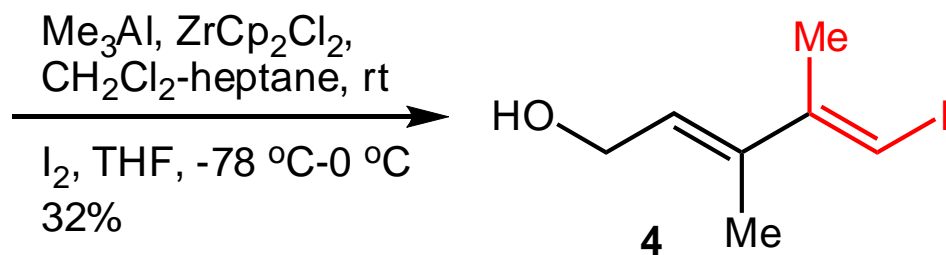
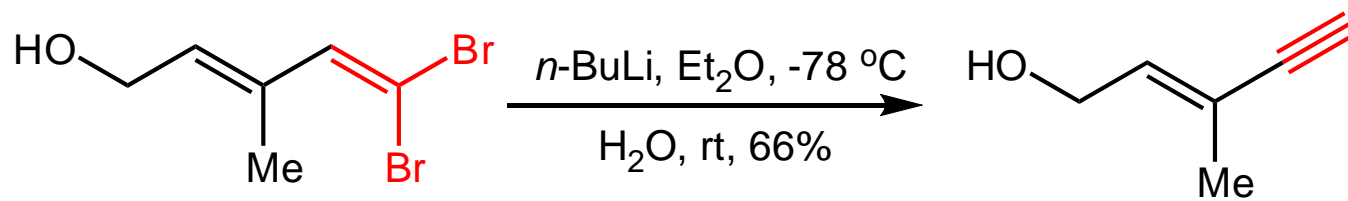




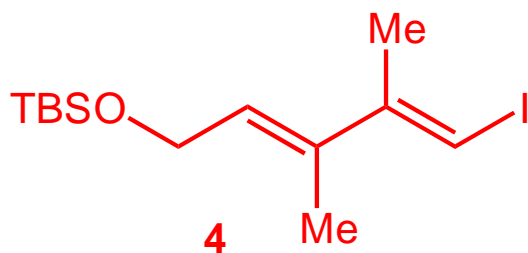
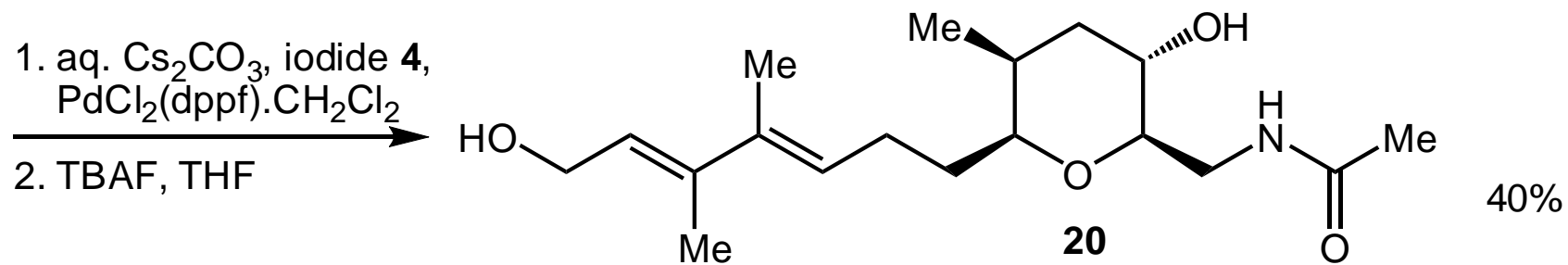
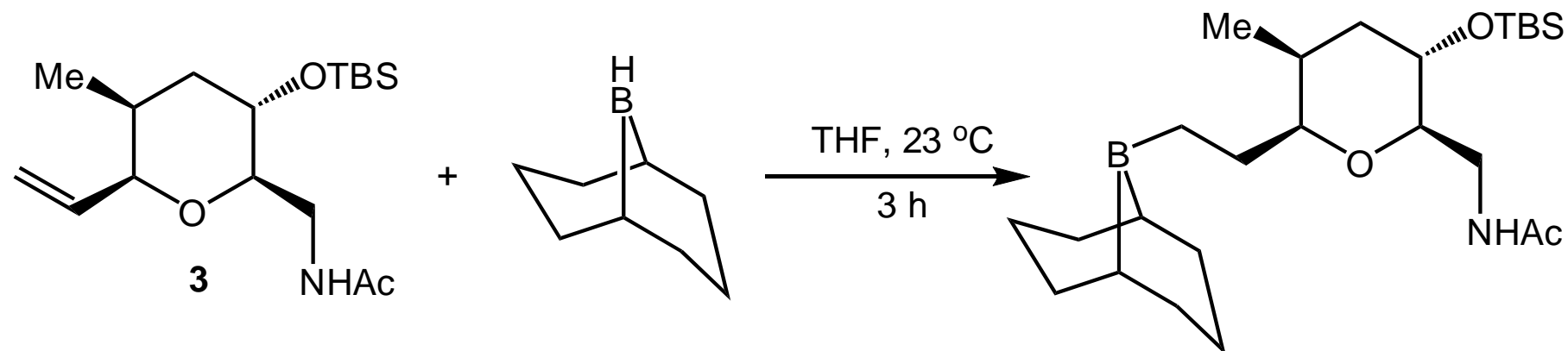


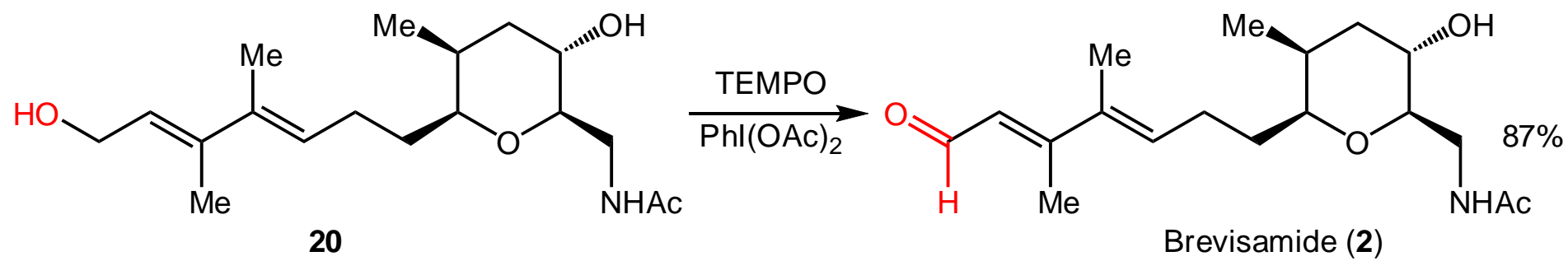


Tachibana, K. *et al.* *Org. Lett.* **2009**, 11, 217-220.



Tachibana, K. *et al. Org. Lett.* **2009**, 11, 217-220.





The bloom of dinoflagellates causing “Red Tide” has led to the massive death of a wide range of marine life and human food poisoning in the Florida Coast and Gulf of Mexico. Brevetoxins secreted by the dinoflagellate *Ptychodiscus brevis* may have been responsible for this extensive natural calamity. In 1981, Nakanishi and co-workers reported the structure of brevetoxin B, the first member of a new class of structurally extraordinary marine toxins. Brevetoxin consists of 11 contiguous trans fused cyclic ether rings, spectacularly arranged in a “ladder-like” rigid framework. Nakanishi and co-workers subsequently proposed an intriguing biogenetic scheme indicating that brevetoxins may be biosynthesized by a polyepoxide cascade cyclization.

In summary, we have reported an asymmetric total synthesis of (-)-brevisamide in 22 total synthetic steps, with an unoptimized yield of 1.7% in **18** longest linear steps from the readily prepared aldehyde **8**. A substituted tetrahydropyran fragment of brevisamide was synthesized in enantiomerically pure form using Jacobsen's asymmetric hetero-Diels-Alder reaction. This reaction has set three of the four stereocenters of brevisamide enantioselectively. The vinyl iodide fragment **4** was readily prepared using Negishi's zirconium-catalyzed carboalumination-iodination reaction. The synthesis also features Suzuki-Miyaura cross coupling and selective allylic oxidation using TEMPO. The present synthesis will provide access to a variety of structural analogues of brevisamide for further studies.