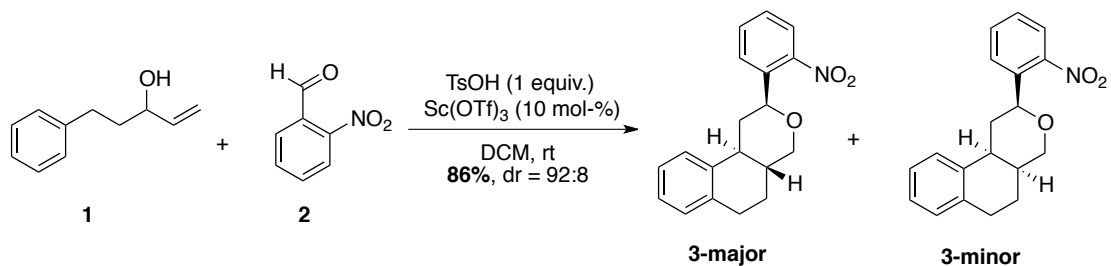


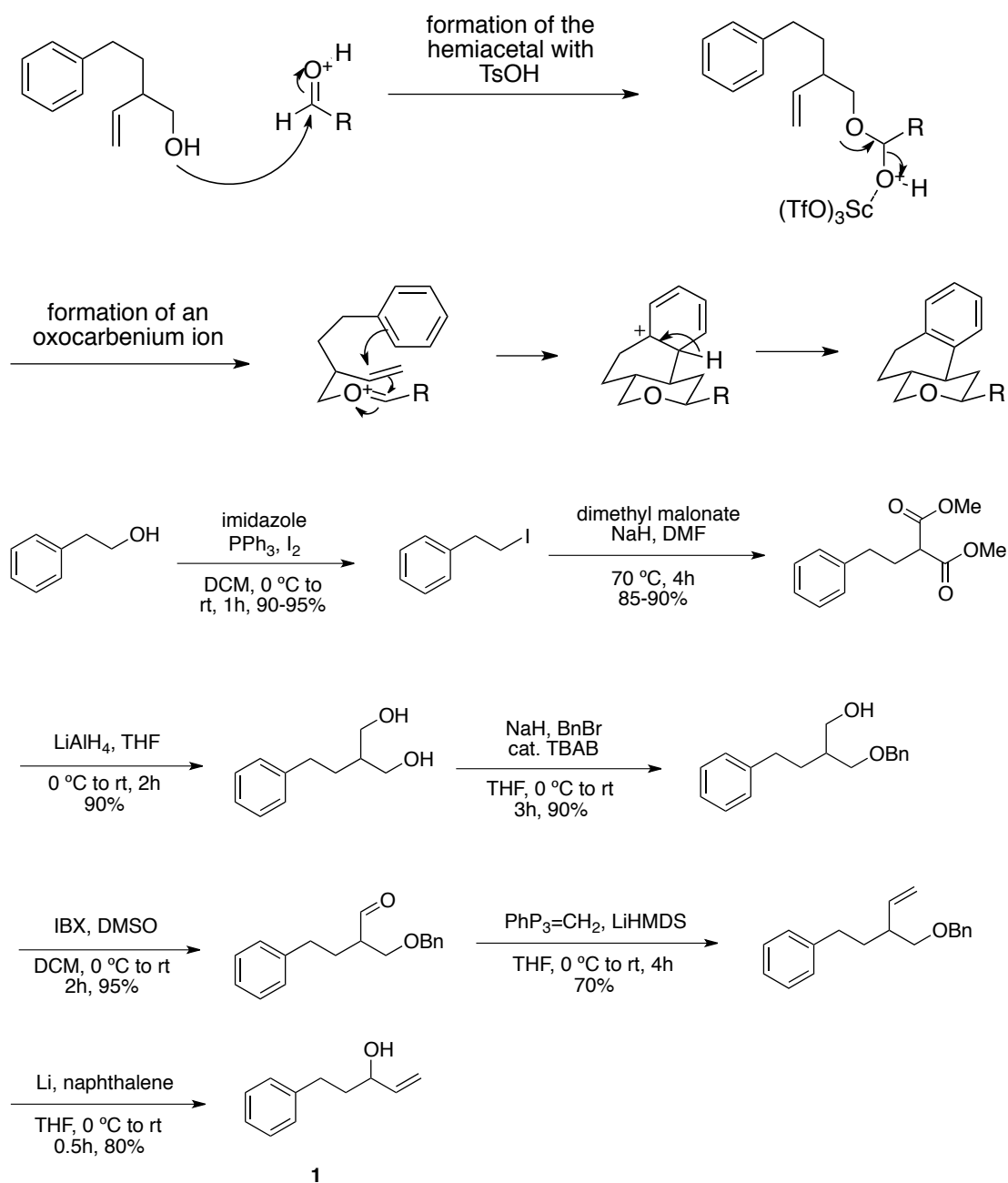
The ??? Cascade Cyclization Reaction for the Synthesis of Angularly-Fused Tetrahydropyran and Piperidine Derivatives

Problem:



- What is the name of the reaction cascade?
- Give the reaction mechanism and explain the diastereoselectivity for the transfused product.
- Give a possible synthesis for **1**.

Hint: - 7 steps starting from 2-phenyl-ethanol

Solution:**Comments:**

The formation of the minor cis-fused product might occur through trapping of the secondary carbenium form the same face as the dihydrostyryl substituent. In this reaction, the Bronsted acid activates the aldehyde to generate the hemiacetal from the aldehyde and a homoallylic alcohol whereas the Lewis acid facilitates the olefin cyclization as well as a Friedel-Crafts reaction. Therefore, both Bronsted and Lewis acid are essential to facilitate the reaction.

The cyclization reaction could also proceed through a 3,3-sigmatropic rearrangement, but the product is as same as the Prins cyclization reaction.

References:

B. V. S. Reddy, H. Kumar, P. Borkar, J. S. Yaday, B. Sridhar. *Eur. J. Org. Chem.* **2013** (Web published: February 2013)

Keywords:

Tandem Prins reaction, transfused tetrahydropuran derivatives