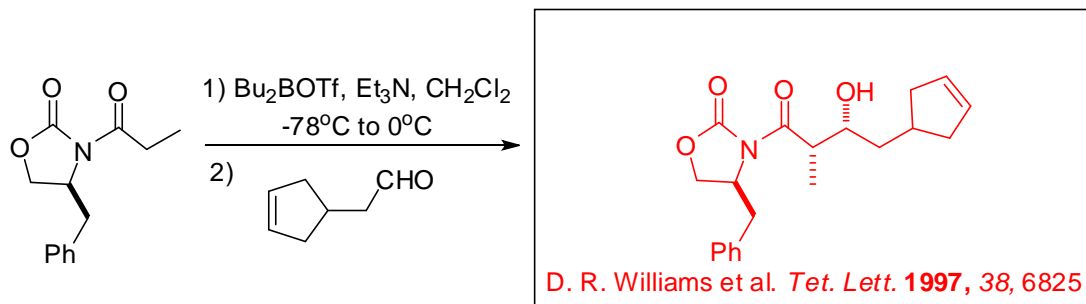
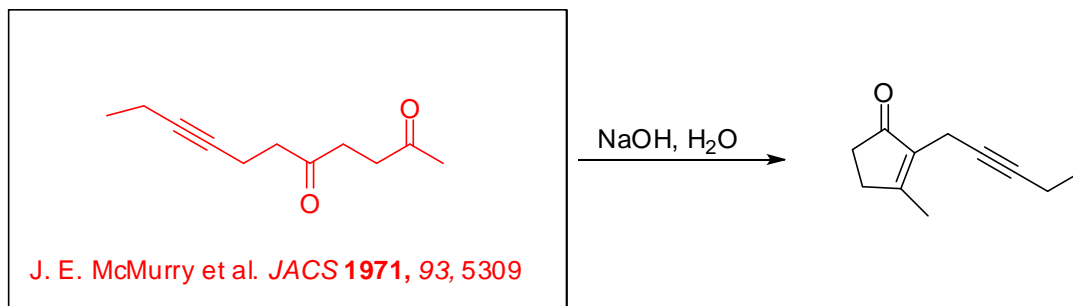


1. Provide the necessary information, products or reagents, to complete the following reactions. Undergraduates must complete three of the four problems and graduate students must complete all four. (4 pts.)

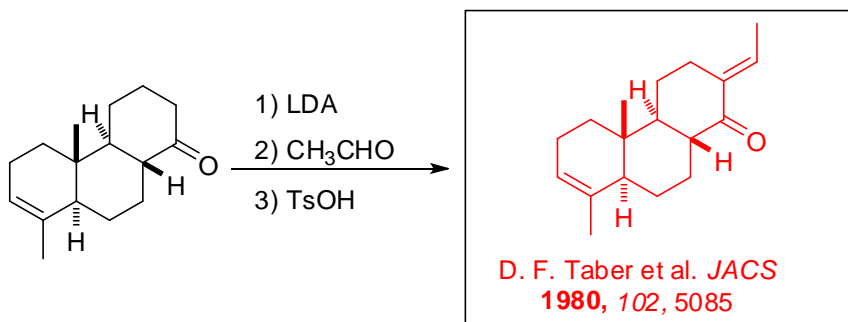
a)



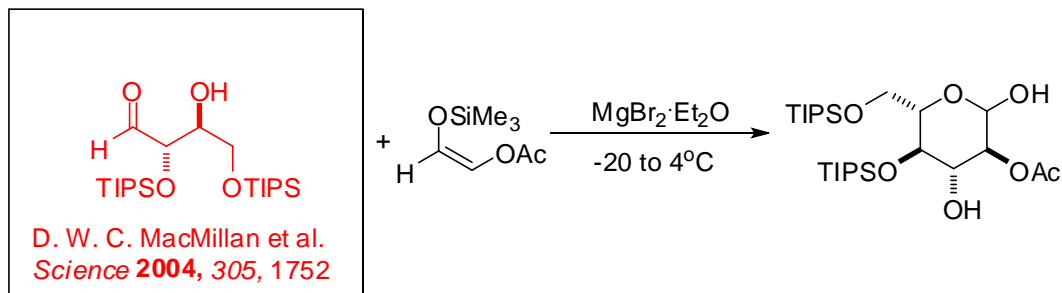
b)



c)

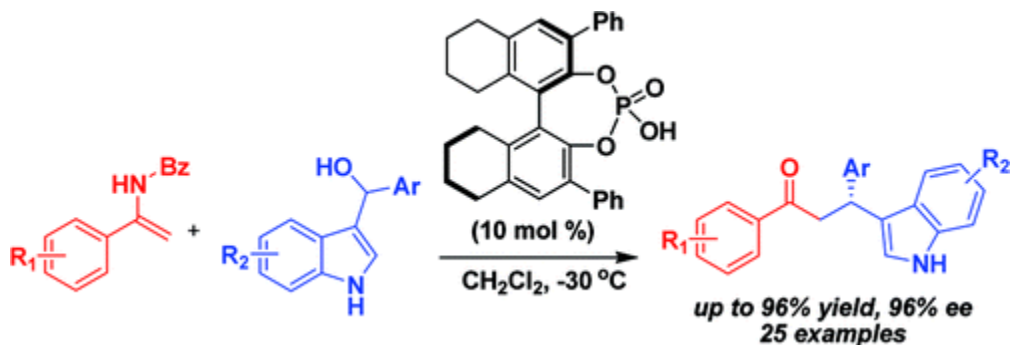


d)



2. Answer the following questions about the recently reported alkylation reaction shown below. (6 pts.)

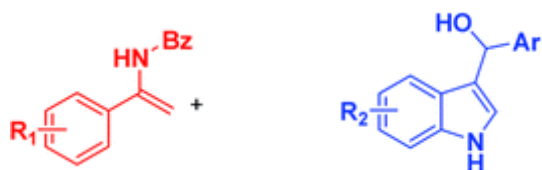
(Qi-Xiang Guo et al. *Org. Letters* **2009**, ASAP, DOI: 10.1021/ol901892s)



a) Identify the nucleophile (Nu) and the electrophile (E+) in the reaction.

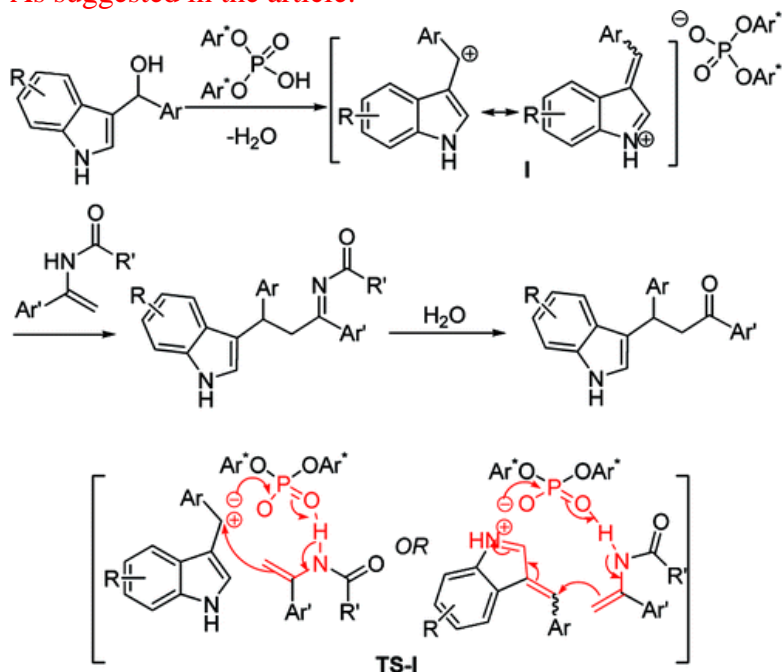
Nu=

E+=



b) Propose a mechanism for the reaction. You may ignore stereochemistry for the mechanism.

As suggested in the article:



c) Both the Nu and the E+ are specialized to work in this reaction. Describe one characteristic of both the Nu and the E+ that makes them well-suited to succeed in this reaction.

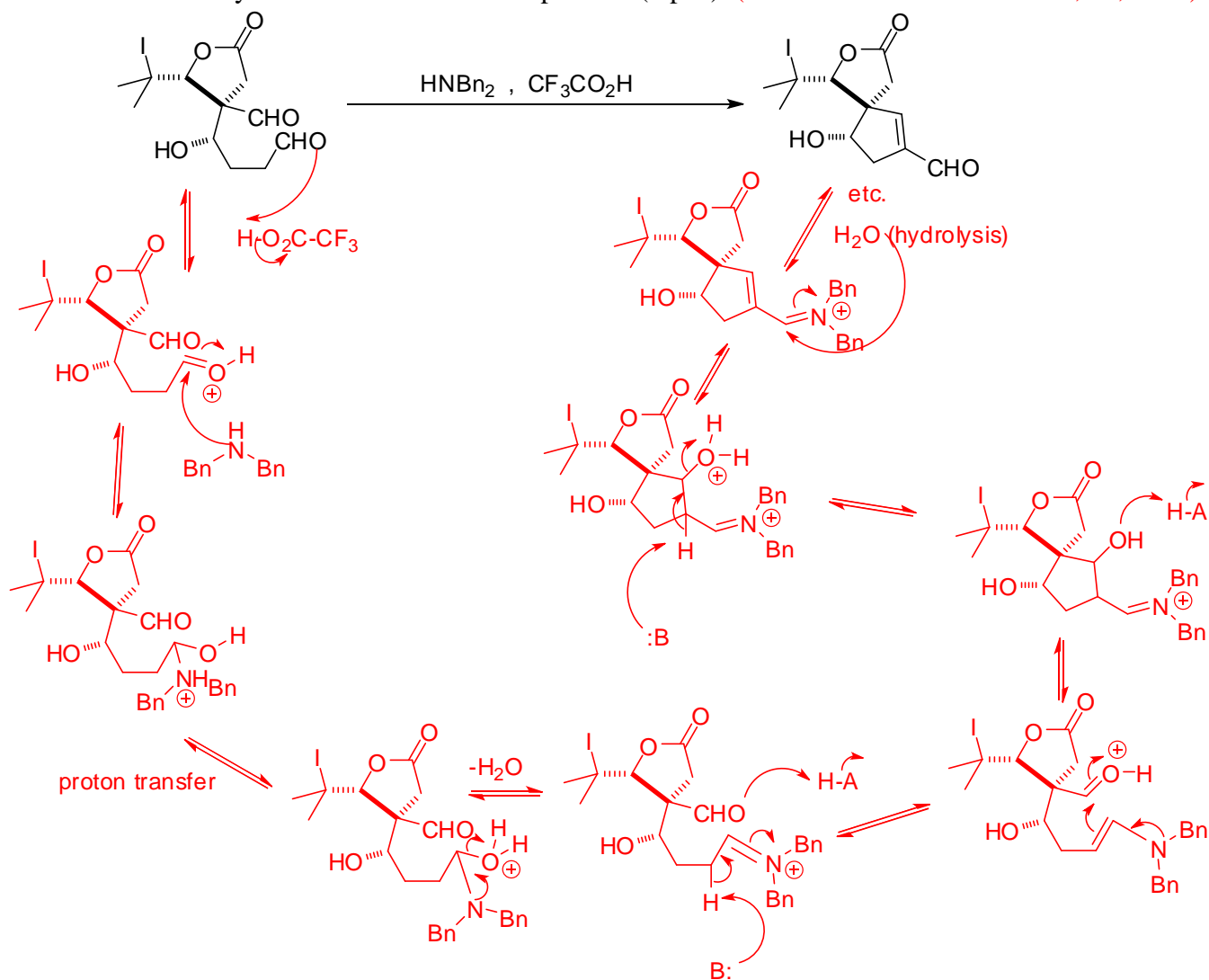
The Nu is an enamide/enamine of a methyl ketone therefore only one enamide/enamine isomer can form. There is no potential for an alternative enamide/enamine regio- or stereoisomer.

The E+ has two aromatic groups substituted on the secondary alcohol which makes the substitution reaction at a doubly benzylic position. This would allow for a particularly reactive secondary C position or a highly stabilized secondary carbocation.

d) Describe the two roles of the phosphoric acid.

The phosphoric acid serves as a proton source to make the alcohol a good leaving group and it is also a chiral catalyst/salt that creates a chiral environment that makes the process stereoselective.

3. Provide a mechanism for the following transformation. You may abbreviate structures for convenience, but be sure the necessary structural information is present. (5 pts.) (B. B. Snider et al. *JOC* 2008, 73, 8049)



4. Natural product synthesis requires an ability to recognize key bond disconnections that can create the requisite carbon framework of a complex molecule. The molecule shown below is the macrocyclic core of the antibiotic erythromycin. It is a polyketide and therefore has a rich collection of potential aldol addition disconnections. Undergraduates must show one bond disconnection and aldol reaction, and graduate students must show two bond disconnections and aldol reactions. Your proposed aldol reactions must control stereochemistry and should afford a structure that can subsequently be incorporated into the product. (5 pts.)

erythromycin macrocyclic core

