THE UNIVERSITY OF TOLEDO 1872

Mid-Term Exam 1

Time: 10:00 am – 10:50 am
Date: February 18, 2016
Room: BO 2059

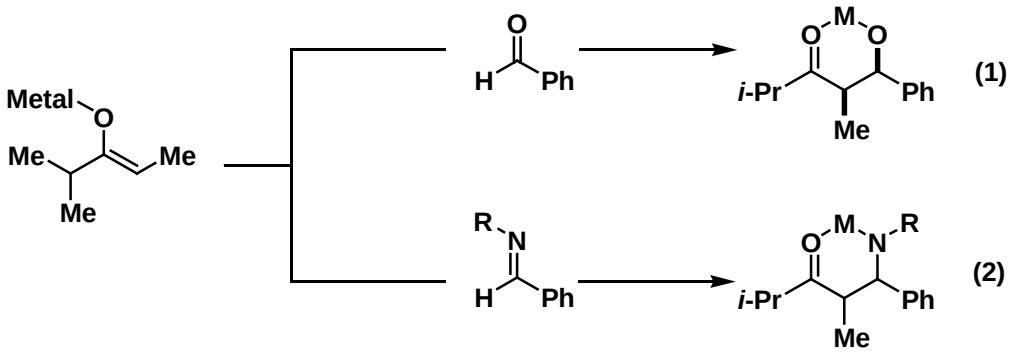
100 Points - Total

1. **Problem:** Please provide mechanisms for 5 of the following 10 named reactions: (**25 PTS**)

1. Sharpless Dihydroxylation
2. Sharpless Epoxidation
3. Swern Oxidation
4. Wittig Reaction
5. Wolff Kishner Reduction
6. Skraup Reaction
7. Stevens Rearrangement
8. Ullmann Reaction
9. Wharton Reaction
10. Tiemann Rearrangement

Answers:

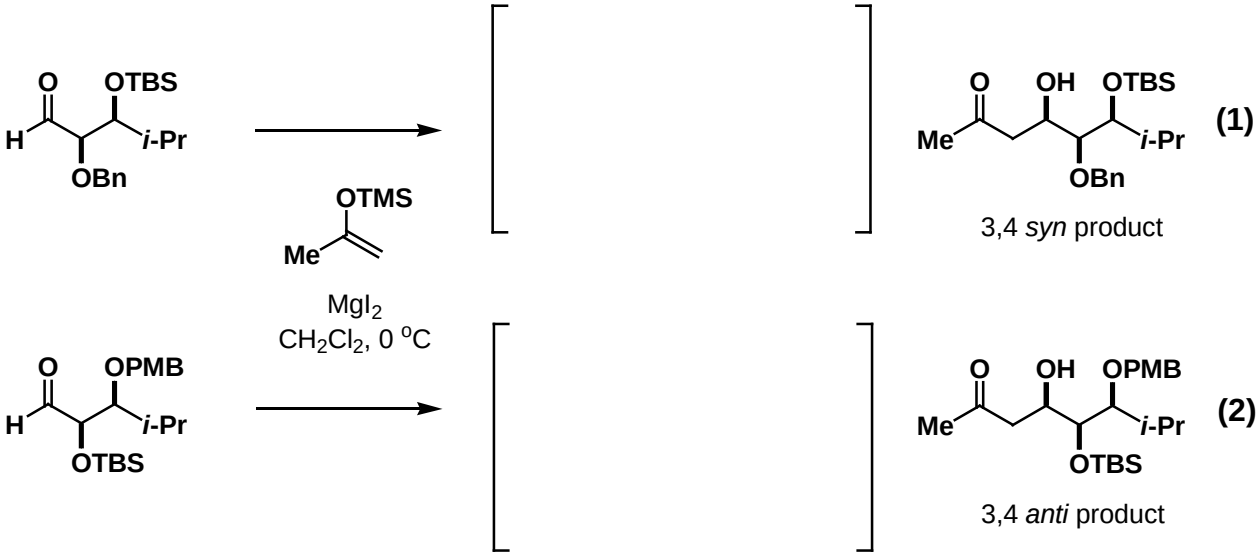
2. **Problem:** The Zimmerman-Traxler transition state nicely correlates starting enolate geometry and product aldol stereochemistry. This point is illustrated in equation 1 below in the correlation of the (Z) enolate geometry with the *syn* aldol product stereochemistry. The intent of this question is to have you ponder the related addition to the illustrated imine (eq 2).



Draw the Zimmerman-Traxler transition state for the "imine-aldol" process (eq 2) and illustrate the predicted stereochemical outcome of the addition reaction. **VERY IMPORTANT**: assume that the imine geometry cannot isomerize under the reaction conditions. (**25 PTS**)

Answer:

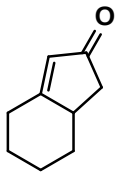
3. **Problem:** The two illustrated MgI_2–promoted Mukaiyama aldol reactions occur with high diastereoselectivity (Eq 1 & 2). In contrast, only poor selectivity is observed in both reactions when MgI_2 is replaced with BF_3•OEt_2. Provide a transition state model that explains the formation of the 3,4 *syn* product in (Eq 1) and the 3,4 *anti* product in (Eq 2). Assume that the Bn and PMB protecting groups are chemically equivalent.



When the chelating protecting group is in the alpha position (Eq 1), a five member chelate is formed and incoming nucleophile attacks the *si*-face opposite to the R group (TS-1). In contrast, a six-membered chelate is formed when the chelating protecting group is in the beta position and the nucleophile approaches from the face away from both the OP and R groups. The observation that BF_3•OEt_2 gives poor selectivity implies that the reaction is not simply under Felkin control, as one may predict for Eq 2. (**25 PTS**)

Answers:

4. **Problem:** Show how you would synthesize the following molecule. Use retro-synthetic analysis to break the pertinent bonds. Provide mechanisms for every step you use. As a hint, start with cyclohexanone and some other compound of your choice (discussed in detail in class). (**25 PTS**)



Answer: