



THE UNIVERSITY OF  
**TOLEDO**  
1872

## CHEM 8410\_6410\_4410 – Organic Synthesis

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### CHEM 8410\_6410\_4410 Spring 2018 – Mid-Term Exam 1 02-13-18

**Time: 10:00am – 11:15am**

**Student Name:** \_\_\_\_\_

**Student Number:** \_\_\_\_\_

<b>Instructor:</b> Prof. Andreana
<b>Room #:</b> FH 2030



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### Mid-Term Exam 1

Time: 10:00 am – 11:15 am  
Date: February 13, 2018  
Room: FH 2030

**100 Points - Total**

1. **Problem 1:** Please provide mechanisms for 5 of the following 10 named reactions: **(25 Points)** - \* indicates this named reaction MUST be one of your 5.

- |                             |                               |
|-----------------------------|-------------------------------|
| 1. 2,3-Wittig Rearrangement | *6. Swern Oxidation           |
| 2. Sandmeyer Reaction       | 7. Skraup Reaction            |
| 3. Wacker Oxidation         | 8. Wharton Reaction           |
| 4. Wolff-Kishner Reduction  | 9. Sharpless Dihydroxylation  |
| 5. Simmons-Smith Reaction   | 10. Schotten-Baumann Reaction |

**Answers:**



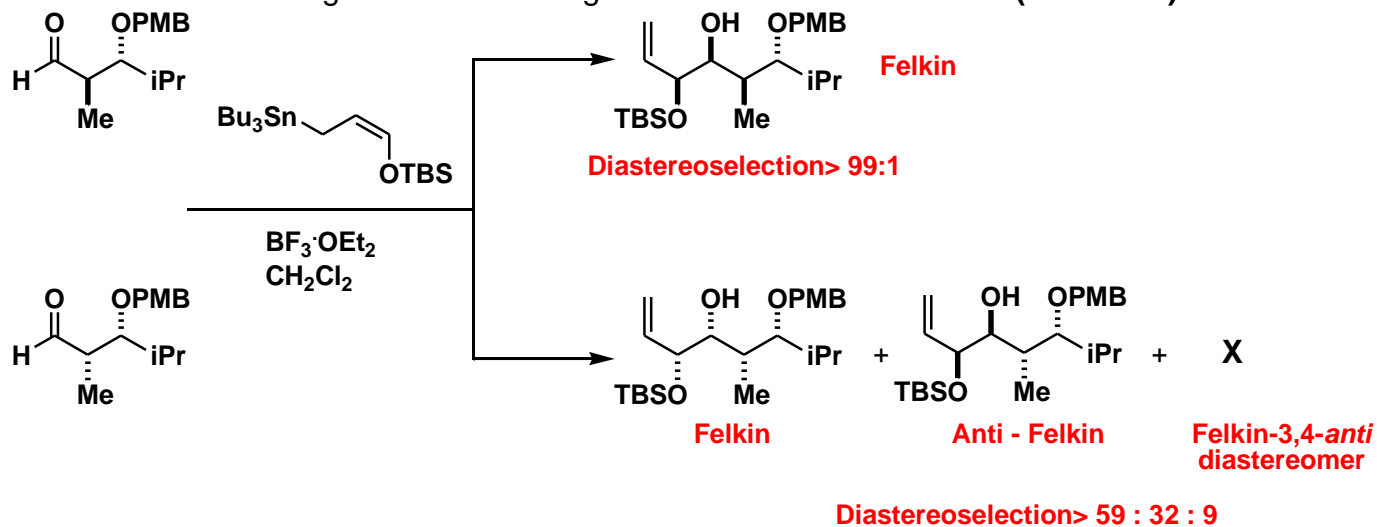
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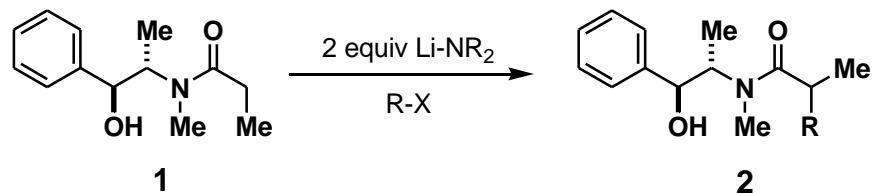
**Problem 2:** Below is an example of nucleophilic addition to carbonyl compounds excepting chelation control. Realize that the two starting materials are *anti* and *syn* leading to a number of products. The *anti* starting material gives almost exclusively one product, however, the *syn* substrate leads to three different products. First you need to show the Newmann projection of the Felkin product then the Newmann projection for the Anti – Felkin. Rationalize why the *anti* vs *syn* can be either reinforcing or non-reinforcing. Provide the structure of X. (15 Points)



**Answers:**



**Problem 3.** The pseudoephedrine-derived propionamide **1**, upon successive enolization with  $\text{LiN}(i\text{-Pr})_2$  (LDA) and alkylation with alkyl halide  $\text{R-X}$ , affords **2** with high diastereoselection (Myers, *JACS* **1997**, 119, 6496).



**Part A.** Enolization of **1** with LDA affords a single enolate geometry. Provide an analysis of this enolization event and draw the enolate thus produced. **(7.5 Points)**

**Part B.** Provide a 3-dimensional drawing of the transition state for this reaction. *Hint: In answering this question, you do not need to assume that chelation is involved. Rather, a suitable transition state model may be derived purely from the consideration of **non-bonding interactions**.* **(7.5 Points)**

**Part C.** Provide the absolute stereochemistry of the alkylation product **2** of this reaction. **(5 Points)**.

**Answers:**



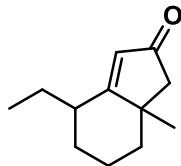
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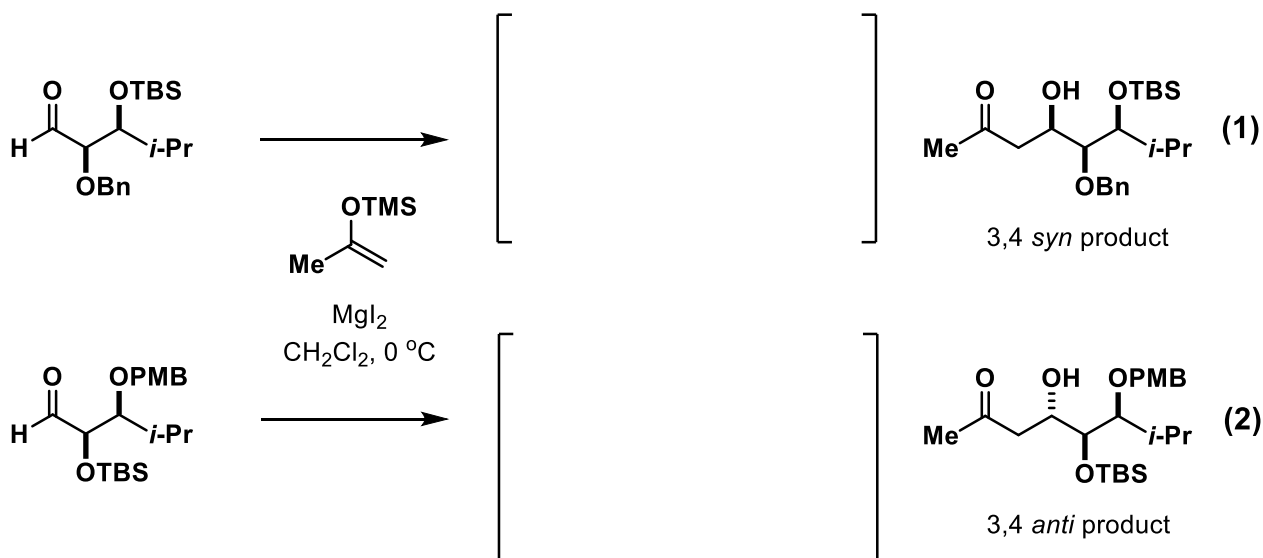
**Problem 4:** Show how you would synthesize the following molecule. Use retro-synthetic analysis to break the pertinent bonds. Provide mechanisms for every step you use. As a hint, start with cyclohexanone and some other compound of your choice (From Quiz #1). (25 Points)



**Answer:**



**Problem 5.** 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  $BF_3 \cdot OEt_2$ . 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. **(15 Points).**



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  $BF_3 \cdot OEt_2$  gives poor selectivity implies that the reaction is not simply under Felkin control, as one may predict for Eq 2.