University of Victoria

Chemistry 432 / 533
Advanced Organic Synthesis
CRN 14026 / 14033

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Instructor: J. E. Wulff

Name: 

Student Number: VO

Time: 3 hours

This exam contains 12 pages, counting the cover sheet.

Please answer all questions within these pages. Scrap paper is provided for rough work, but will not be graded.
Part 1. Provide the product, starting material or reagents (as indicated) for 5 of the following 6 reactions. Specify the stereochemical outcome of the reaction wherever appropriate. If you attempt all 6, be sure to **cross out** the one you don’t want me to mark. Otherwise, I will go in order.

A. $\text{CH}_3\text{C}_6\text{H}_5\text{CHO} \xrightarrow{\text{KH}} \text{CH}_3\text{C}_6\text{H}_5\text{CH(OH)}\text{CHO}$

B. $\text{H}_3\text{C}\text{C}_6\text{H}_5\text{CH(OH)}\text{CHO} \xrightarrow{\text{KH}, 18\text{-crown}-6} \text{H}_3\text{C}\text{C}_6\text{H}_5\text{C}_6\text{H}_4\text{CH(OH)}\text{CHO}$

C. $\text{PhSiMe}_3 \xrightarrow{1. \text{MgBr}} \text{PhPh} \xrightarrow{2. \text{H}_3\text{O}^+} \text{PhPh}$

D. $\text{C}_6\text{H}_5\text{Br} \xrightarrow{\text{PhSiMe}_3} \text{C}_6\text{H}_5\text{SiMe}_3$

E. $\text{(Cyclohexyl}_3\text{P})_2\text{RuCl}_2\text{CHPh} \xrightarrow{\text{H}_2\text{CCH}_2} \text{C}_6\text{H}_5\text{SiMe}_3$

F. $\text{H}_3\text{C}\text{O}_2\text{SO}_2\text{O} \xrightarrow{\text{Rh}_2(\text{esp})_2, \text{PhI(OAc)}_2 / \text{MgO}}$
In a 2004 paper, Alan Armstrong's group (Imperial College, London) reported the reaction of "tosyl nitrene" (generated in situ from chloramine-T) with dihydropyran 1. Rearrangement was observed, leading to the formation of pyrrolidine 2. Propose a mechanism for this transformation.

Note: Don't worry about rationalizing the stereochemistry. The products in this case would epimerize on the column to provide the most thermodynamically stable diastereomer.
In a followup paper, Armstrong reported that the addition of vinyl Grignards to 2 resulted in intermediates (3) that were capable of further rearrangement. Treatment of 3 with 1 equivalent of \( \text{SnCl}_4 \) at 0 °C for 8 minutes resulted in the formation of azabicyclo[2.2.1]heptane 4. Propose a mechanism for the conversion of 3 into 4.

Note: There are actually two reasonable mechanisms for this step. You only need to come up with one of them for full marks.
Addition of excess tin chloride, and warming of the reaction mixture to room temperature, led to yet another rearrangement, this time resulting in the formation of tropanone 5. Propose a mechanism for the evolution of 4 into 5.
Part 3. The following synthesis of ibogamine was completed by James White’s group in 2000. Fill in the blanks corresponding to reagents or intermediates where indicated. For the two requested mechanisms (A and B), please write your responses on the subsequent pages. In one case, I have used a blue circle to highlight where the molecule has been transformed. In other steps, I have left the products unannotated, so you will need to figure out for yourself what reaction has taken place.
Space for mechanisms is provided on the next two pages.
Mechanism for Step A:
Mechanism for Step B:
Part 4. Propose an **enantioselective** synthesis for 2 out of the following 4 natural products. Your approach should begin with commercially available reagents. You can assume that you have access to:

(a) **simple** alkyl, alkenyl or alkynyl reagents with up to 4 carbon atoms, for example:

\[ \text{alkyl, alkenyl or alkynyl reagents} \]

(b) aryl or heteroaryl molecules with a **maximum of 2 simple substituents** (each containing ≤ 1 carbon atoms), e.g.:

(c) **simple** 5- or 6-membered rings, for example:

(d) other reagents or catalysts that we’ve seen in class.

You will **not** have access to organotin or organoborane compounds, so you’ll have to make those yourself.

Please write your final answers on the next two pages – I’ve also provided some scrap paper you can use for working through your ideas, but this will not be submitted with your exam so make sure you have something good in the allotted space.
Synthesis #1: