

Answer Key

There are 100 points on the exam.

There are four questions (and six pages to this PDF).

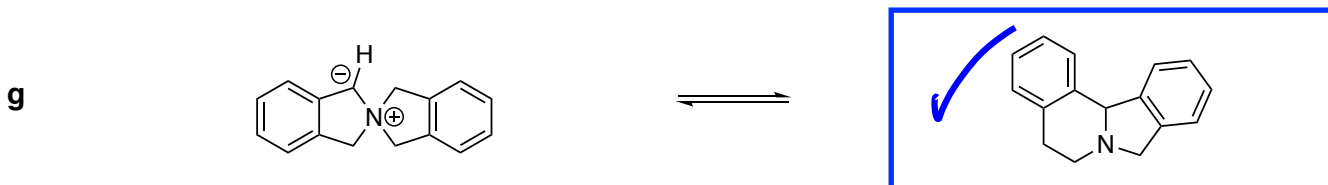
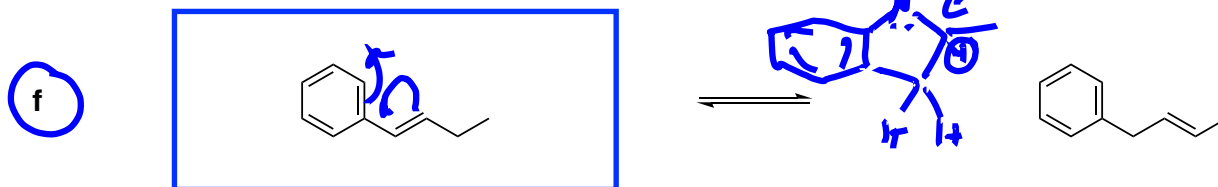
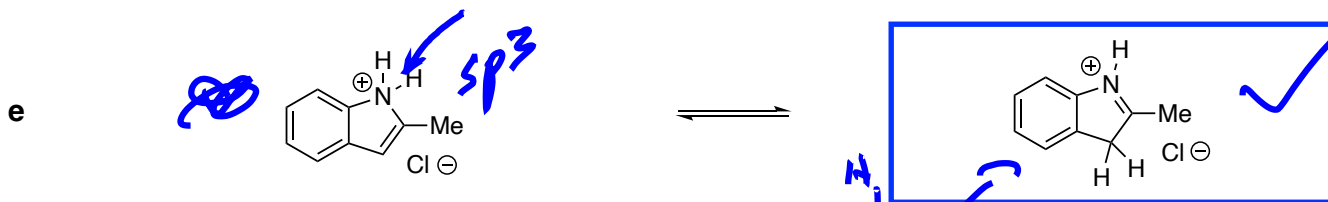
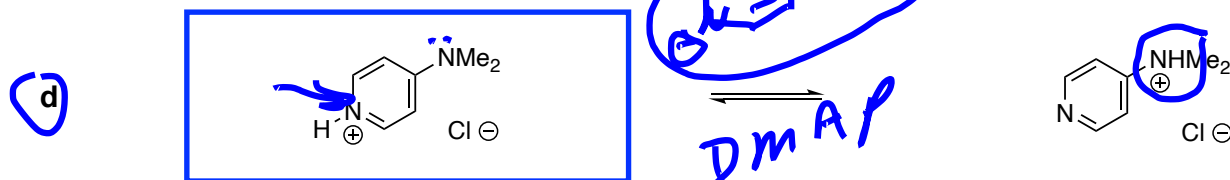
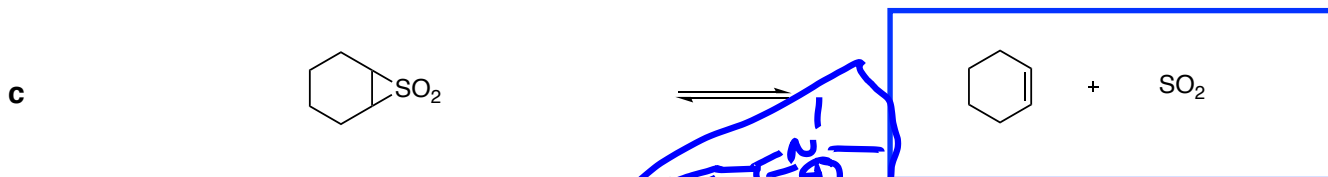
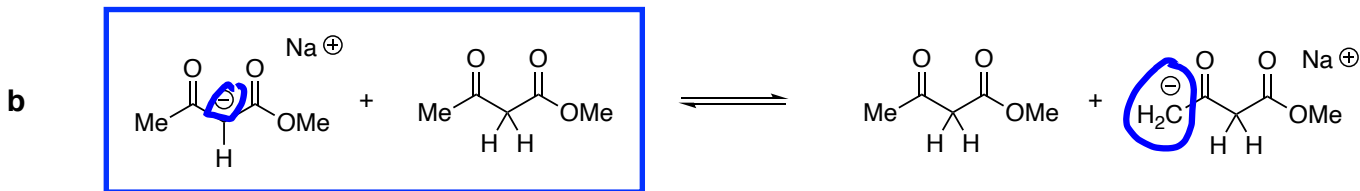
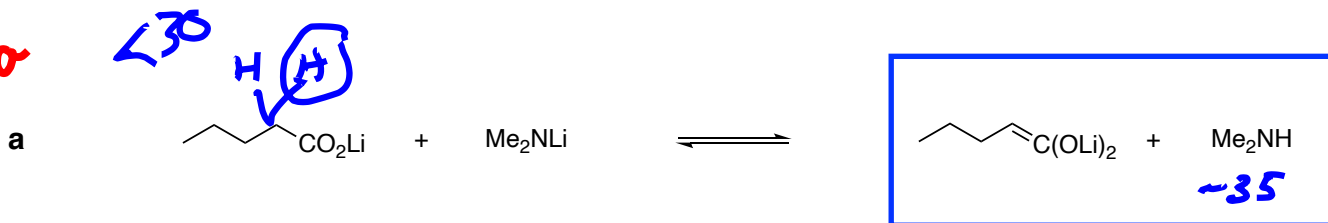
Part I	<u>14 / 14</u>
Part II	<u>16 / 16</u>
Part III	<u>21 / 21</u>
Part IV	<u>49 / 49</u>
Bonus	<u>04 / 04</u>
Total	<u>104 / 100</u>

Instructions

- Print your name at the top of your first sheet of answers **and add your signature**.
- Your **signature will attest** to the following statement:
"I have not communicated with any other person about this exam during the exam period."
- Answer all questions either on
 - i) blank sheets of paper
 - or, if you are comfortable doing so,
 - ii) by electronically entering your answers directly on this PDF.
- **If i)**, please clearly label the number of each of your answers the same as that of the problem (e.g., III.b.).
- Refrain from the temptation to provide long answers just because you have unlimited room.
- This exam is "open book" and "open resource." That is, you may consult books, the internet, your notes, previous problem sets and answers, Reaxys, etc. – but not another human.
- The only exception is that you may consult with Dorian by email (snedd011@umn.edu) if you have a question about the clarity or meaning of any of the questions themselves.
- When finished, please number all pages of your answer sheets in the top-right corner (e.g., 1 of 5, 2 of 5, etc.).
- **If i)** scan (if possible) or carefully photograph each page (check the readability of those images) of your answers and assemble into a PDF or
if ii) simply save the PDF in which you have inserted your answers.
- Assemble all electronic files into a single PDF, if possible, naming it YOURLASTNAME_Midterm-II.
- Upload your answers to the Midterm-II folder Dorian has placed in your Google Drive home folder by 8:15 pm.

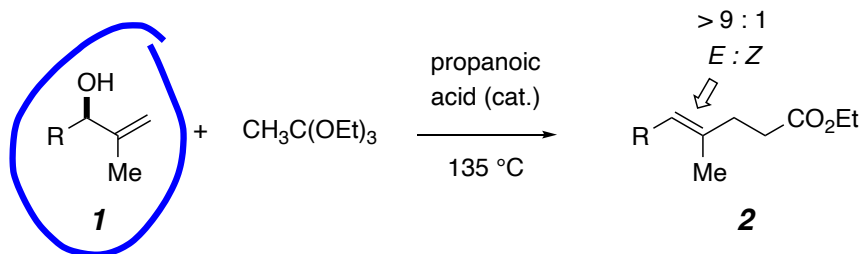
I. (14 points) Decide whether each of the following equilibria lies predominantly to the **left** or to the **right**. Answer "right" or "left" for each of **Ia–Ig** on the exam answer sheet you are creating (or simply circle your answer on the PDF itself).

2 ea.
2 ea.

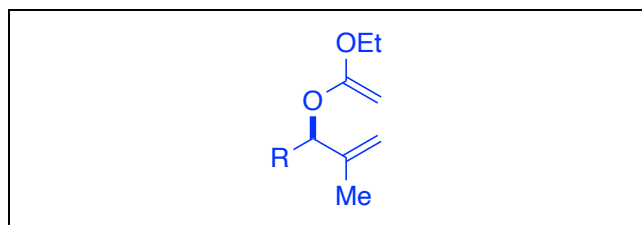


STEREON.

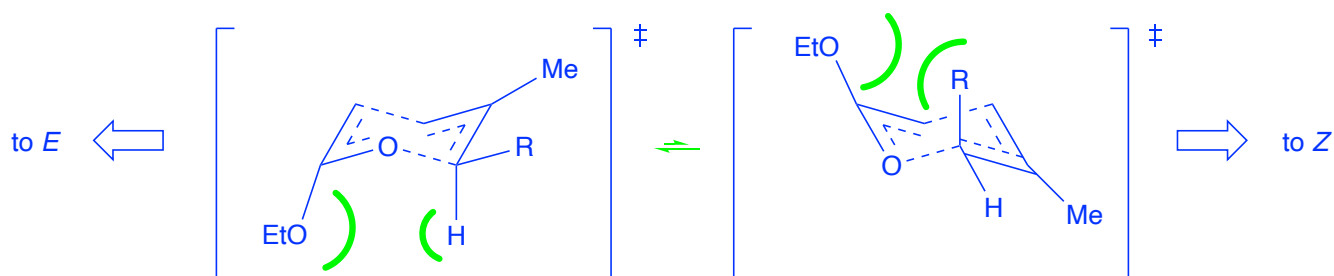
II. (16 points) The Johnson orthoester Claisen rearrangement of appropriate allylic alcohol substrates is an excellent method for stereoselective formation of trisubstituted alkenes. For example, chiral, secondary alcohol substrates like **1** show a preference for formation of the product **2** in which the major alkene product has the *E*-geometry. When **1** is treated with triethyl orthoacetate and an acid catalyst, the product ratio of *E*:*Z* alkenes is typically >9:1.



- a) Provide the structure of the key reaction intermediate within which the [3,3]-sigmatropic (Claisen) rearrangement occurs during the conversion of **1** to **2**.



- b) Show the geometry of two transition states, one that leads from the structure of the intermediate you answered in a) to the *E*-alkene and a second that leads from that same intermediate to the *Z*-alkene. Use the chair-like templates provided below. Think carefully about where to place the stereogenic allylic carbon atom (and its H and R substituents) in substrate **1** onto these transition state structures.

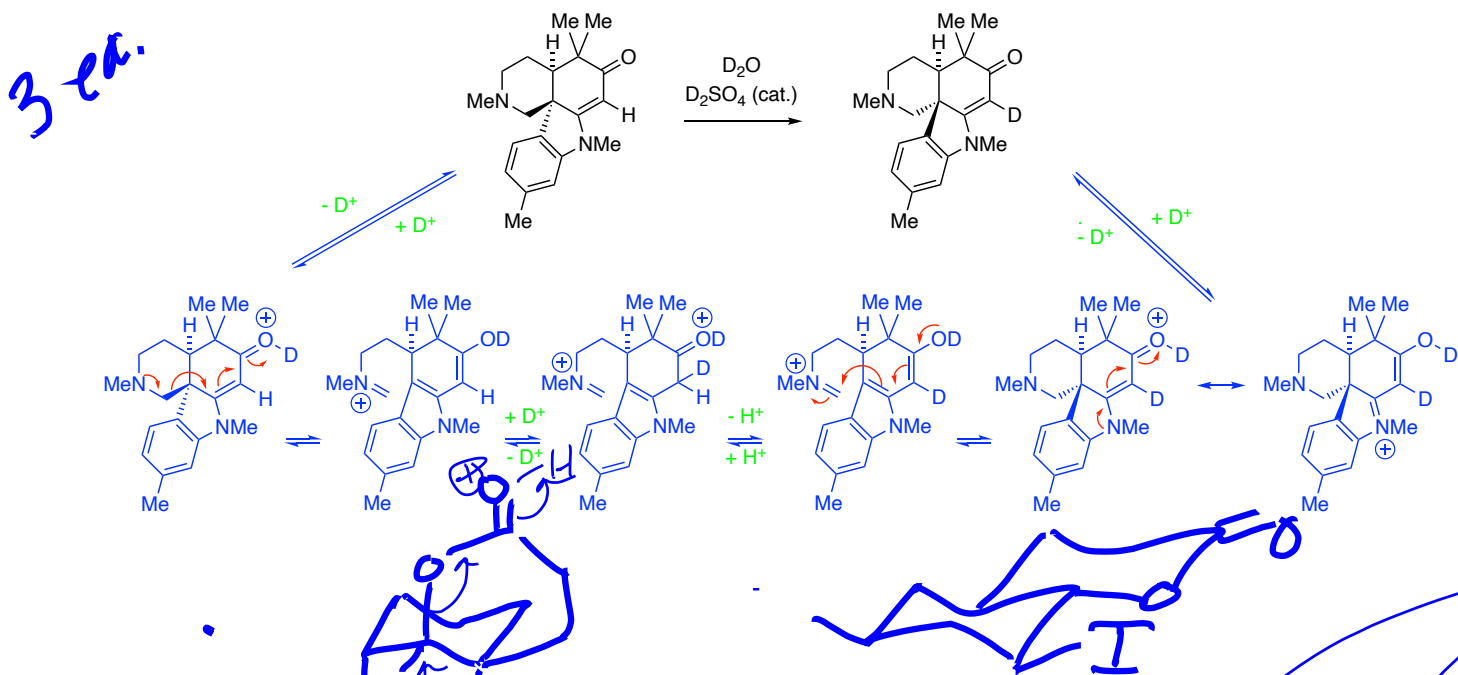


- c) In 1-2 sentences, suggest the specific reason for preferential formation of the *E*-alkene (i.e., what structural feature(s) render(s) one of the two transition states to be more stable?).

The quasi-chair-like geometry of the two different transition state geometries differ in that the one on the left, which leads to the *E*-product, has the R group in an equatorial orientation but it is axial like in the righthand TS_Z . The ethoxy group is pseudo-axial and greater steric repulsion in TS_Z makes it higher in energy, which translates to a higher activation barrier and slower reaction.

IV. (49 pts) Provide a *detailed mechanism* to account for each of the following four reactions. Show *ALL* intermediates, equilibria, and bond-making and -breaking steps.

a) (18) The epimerization of this cis-fused tetracyclic enone to the trans-fused diastereomer (*hint: think retro vinylogous Mannich reaction*).



b) (10) The epimerization of this cis-fused iodolactone to the trans-fused diastereomer

