CH 336
Midterm Exam 3
Friday, May 27, 2005

Printed Name:_____
Before you begin, please verify that you have all 7 pages of the exam and write your name on each page.
Show all your work if you wish partial credit.
Good Luck!!

This is a closed book examination. You may not use any notes, books or external materials except for molecular models during the course of the examination.

On my honor, I have not given or received aid during this examination

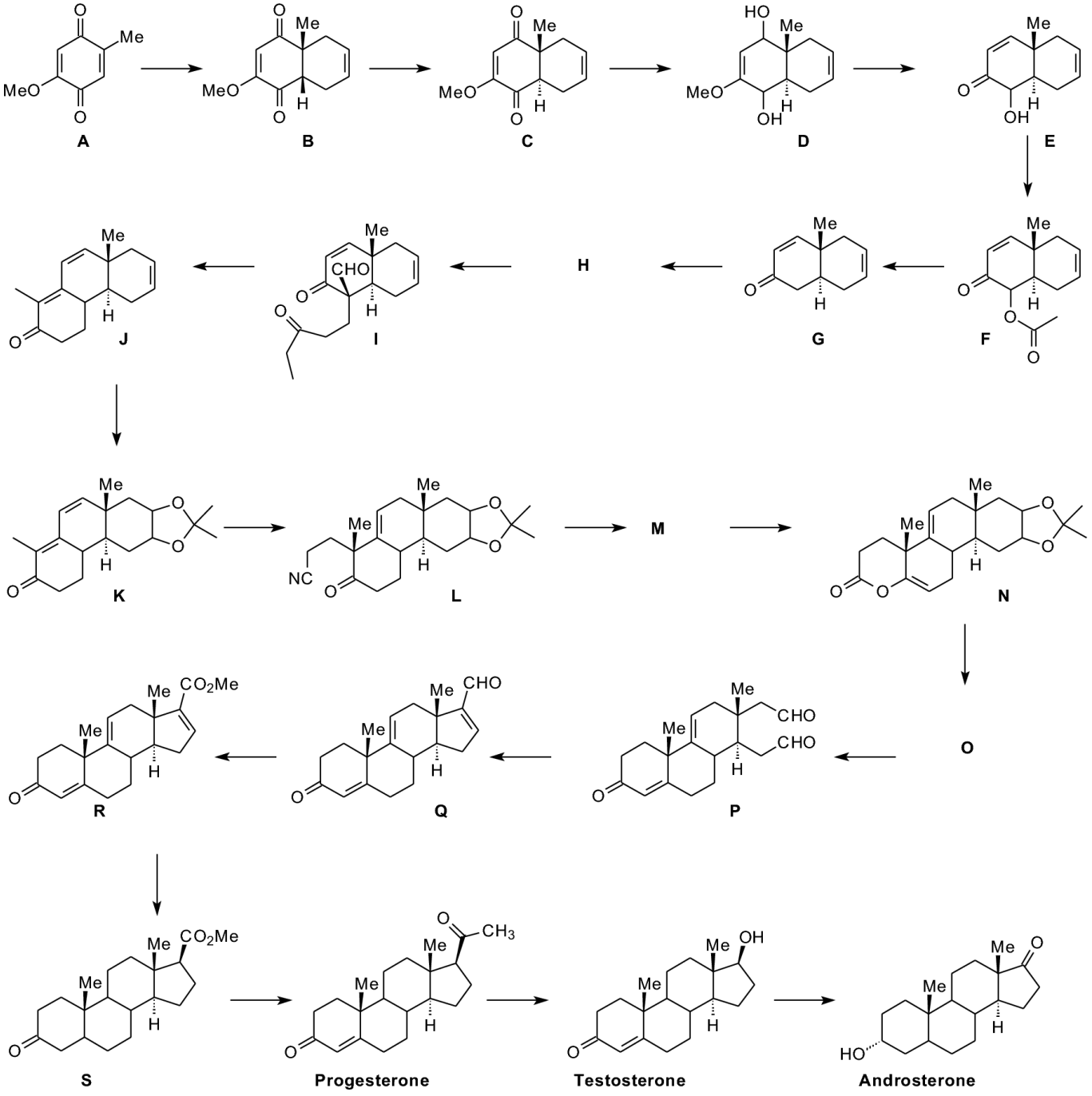
Signature_____ ID _____

Grading:	Section I	(20 points) _____
	Section II	(35 points) _____
	Section III	(20 points) _____
	Section IV	(25 points) _____
	Total	(100 points) _____

Form B

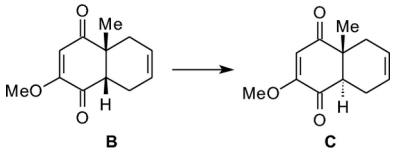
Steroids are important biological compounds that are used, in part, as chemical signaling agents by the body. In 1952, the esteemed synthetic organic chemist R. B. Woodward and several students published the following synthesis of several important steroids that you may recognize as human sex hormones. While the synthesis itself and the molecules involved are quite complex, all of the individual reaction steps involve chemistry that we have discussed in this course. All of the questions on this exam will refer to this synthesis. You will be shown structures that relate to specific questions.

Be careful to focus on where reactions are occurring; do not get overwhelmed by the complexity of the molecules!



I. Multiple choice problems (4 points each). Circle the letter of the best response to each question.

1. Conversion of **B** to **C** requires:



A. Demethylation with I^- and realkylation of the enolate

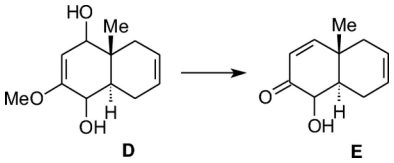
B. Deprotonation to form the enolate and reprotonation

C. Reversal of the Diels-Alder, and readdition to form the exo product

D. Reduction of the carbonyls and reoxidation.

Ref: Pr. 22-3, 22-61

2. Conversion from **D** to **E** involves two sequential reactions using the same reaction conditions. The best way to do this is:



A. p-TsOH and water.

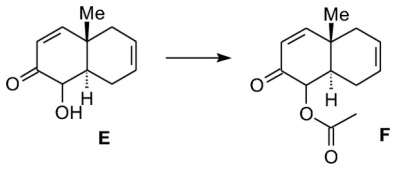
B. Strong base.

C. Zn(Hg) amalgam, HCl

D. Chromic acid.

Ref: Class discussion (enol ethers)

3. Select the best reagent(s) for converting **E** to **F**.



A. Diazomethane.

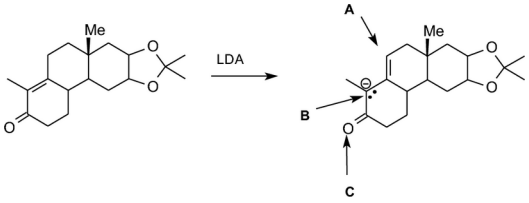
B. Acetamide and concentrated sulfuric acid with heat.

C. Acetic anhydride and pyridine

D. Lithium diisopropylamide in ethanol.

Ref: Pr. 21-47a; Quiz 7 #6

4. In converting **K** to **L**, Woodward first hydrogenated one of the double bonds, to form the enone shown below, then deprotonated. Select the answer that indicates the nucleophilic site(s) in the deprotonated enolate product.



A. Site A

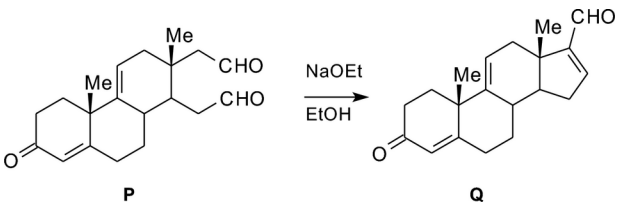
B. Site B

C. Site C

D. All three sites are potential nucleophiles because of resonance.

Ref: Pr. 22-61 f, g, h; Quiz 8, #1

5. Conversion of **P** to **Q** has which competing side reaction:



A. Aromatization of the ring containing the enone.

B. Ketal formation.

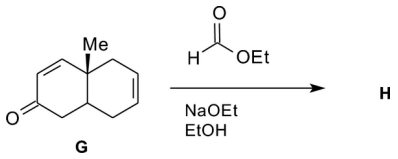
C. The opposite cross-aldol condensation.

D. Oxidation of the ketone.

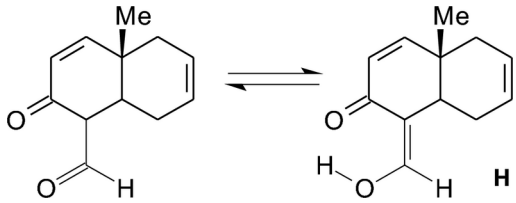
Ref: Sec. 22-9, 22-10; Quiz 8, #8

II. Fill in the blank (5 points each).

6. Conditions for conversion of **G** to **H** are shown; draw the structure of **H**.

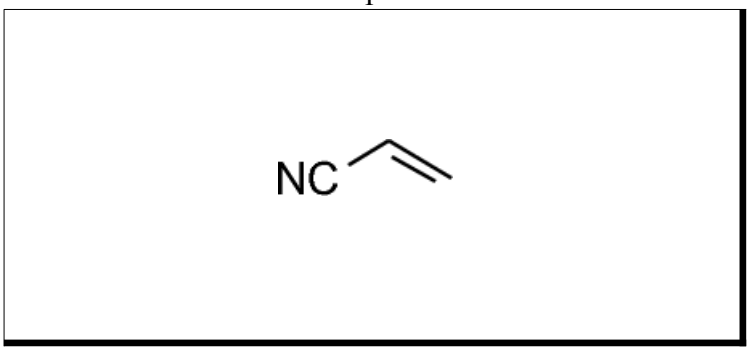


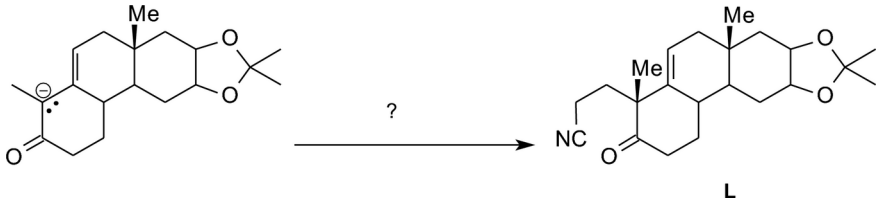
Ref: Pr. 22-73a



Either tautomer is acceptable

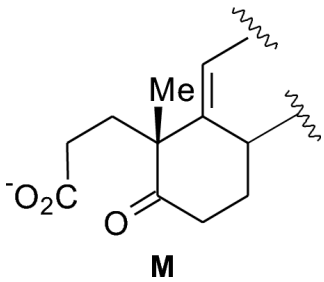
7. Conversion of **K** to **L** is a two-step reaction requiring a Michael addition in the second step. Draw the structure of the molecule that acts as the Michael acceptor.



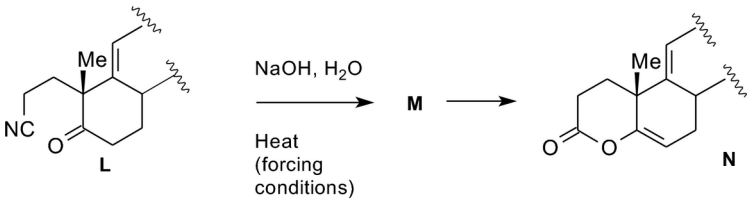


8. Conversion of **L** to **N** involves an intermediate **M** that readily cyclizes under the right reaction conditions. Draw this intermediate. (Note: you need not draw the entire molecule, but may abbreviate it as I have in the equation below so long as you show the correct functional groups.)

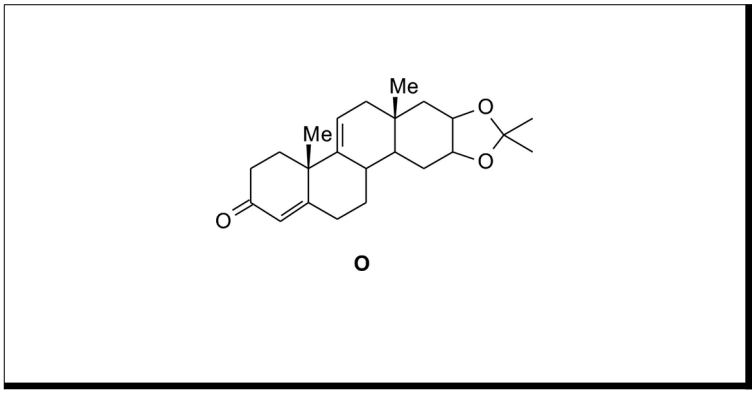
Ref: Class discussion
Michael acceptors
(somewhat: Quiz 8 #5)

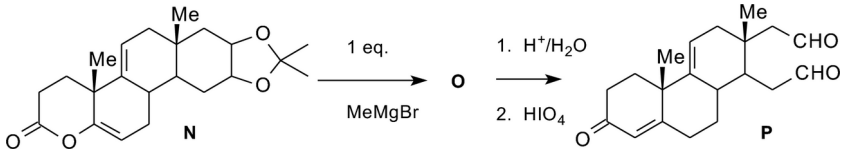


The carboxylic acid is also acceptable for full credit, though under the reaction conditions it will be deptotonated.

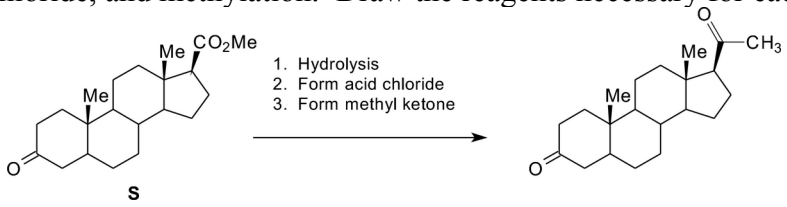


9. Conversion of **N** to **O** is accomplished with one equivalent of methylmagnesium bromide, while **O** to **P** is centered on cleaving the ketal and oxidizing the resulting diol. Draw the structure of **O**. (Please draw the full molecule.)





10, 11, 12. Conversion of **S** to progesterone involves a 3-step process requiring hydrolysis of the ester, formation of an acid chloride, and methylation. Draw the reagents necessary for each step.



10. Ester Hydrolysis:

Either $NaOH/H_2O$

or H_3O^+

Ref: Pr. 21-49 b, c, d

Quiz 6 #6

11. Formation of Acid Chloride:

Either $SOCl_2$ or ClCOCOCl (oxalyl choride)

Ref.: Pr. 20-35c

Quiz 6, #7

12. Formation of Methyl Ketone:

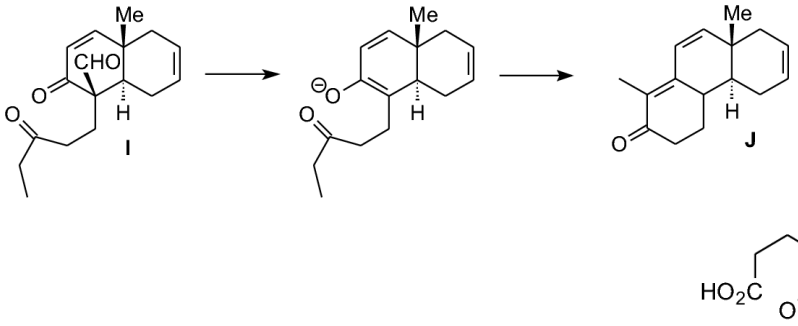
Me_2CuLi

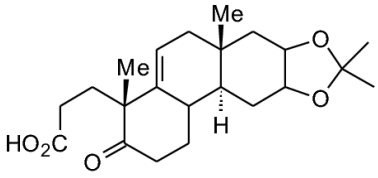
-3 for MeMgBr

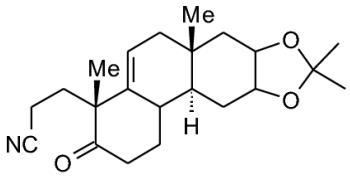
Ref.: Class discussion

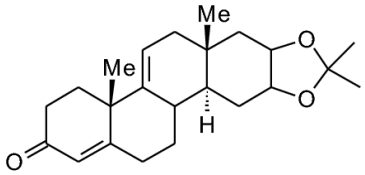
III. Mechanism.

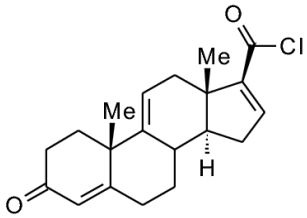
Conversion of **I** to **J** involves a retro-Claisen condensation followed by completion of the Robinson annulation.

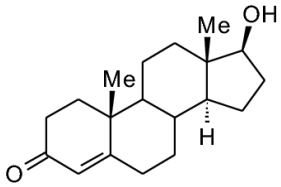




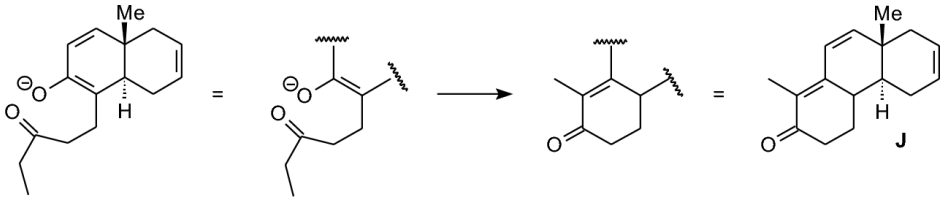


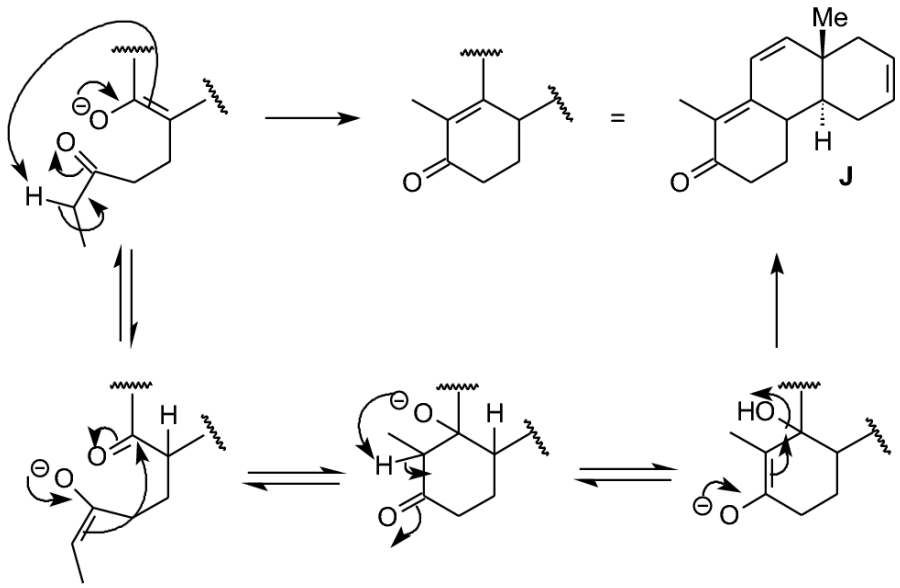






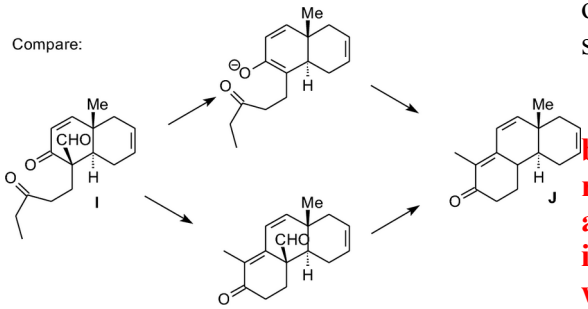
13. (15 points) Write the mechanism for the Robinson annulation (shown) under basic conditions.





Ref: Pr. 22-73 c, d

14. (5 points) Explain whether it matters in which order the retro-Claisen and the Robinson annulation occur. You may use one or two sentences, and you may add structures or equations to illustrate your point.



To a first approximation, no, it does not matter because the retro-Claisen reaction will still form a resonance-stabilized carbanion if the Robinson annulation occurs first. However, note that the aldehyde is a better electrophile than the enone carbonyl; this would provide a selectivity issue for C-C bond formation in the Robinson, and is in fact the reason the retro-Claisen occurs first.

IV. Spectroscopy.

15. (20 points) Match IR spectra with the appropriate synthetic intermediate. The spectroscpic data is only a partial listing that covers important structural components. Place the letter for the spectral data in the box next to the structure that best fits it. For possible partial credit, include how you assign each piece of data to specific structural features.

Spectoscopic information: Structures:

A. IR:1770 cm^{-1}, 1680 cm^{-1}.
^1H NMR: three vinylic peaks (6.2, 5.3, 4.8 ppm).
No peaks disappear on adding D_2O.

D

B. IR: 1680 cm^{-1}.
^1H NMR: two vinylic peaks (5.2, 4.8 ppm)
No peaks disappear on adding D_2O.

C

C. IR: 1720 cm^{-1}, 2235 cm^{-1}.
^1H NMR: one vinylic peak (5.2 ppm)
No peaks disappear on adding D_2O.

B

D. IR: Broad peak 3200-2500 cm^{-1}; 1720 cm^{-1}, 1710 cm^{-1}.
^1H NMR: one vinylic peak (5.2 ppm)
one very broad peak (10.8 ppm) that disappears on adding D_2O.

A

E. IR: 3300-3500 cm^{-1}, 1680 cm^{-1}.
^1H NMR: one vinylic peak (4.8 ppm),
one peak (2.8 ppm) that disappears on adding D_2O

E

Ref.: Table 21-3, Pr. 21-4
Quiz 7, #2