Chemistry 547 (Reich)

First Hour Exam

Oct. 17, 2013

Question 1 _____/32

2 _____/16

3 _____/25
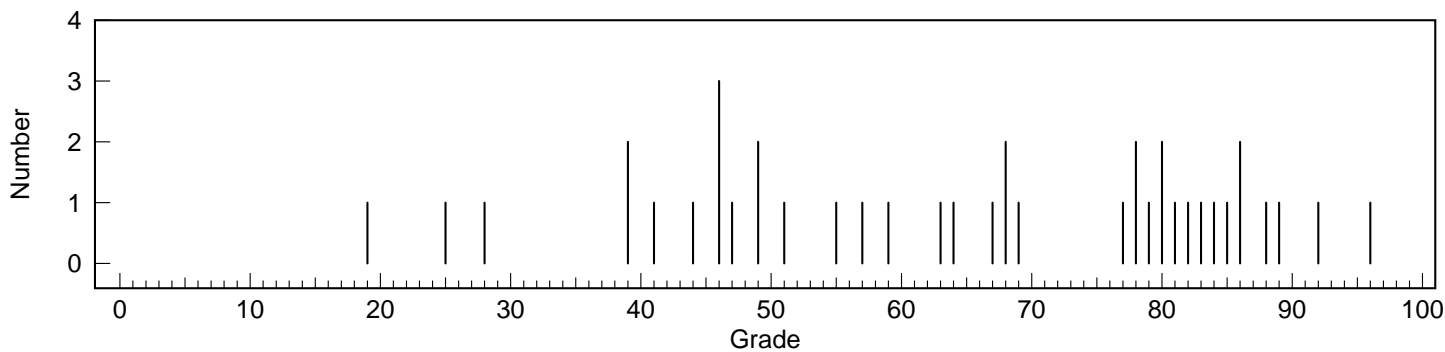
4 _____/20

5 _____/7

Total _____ /100

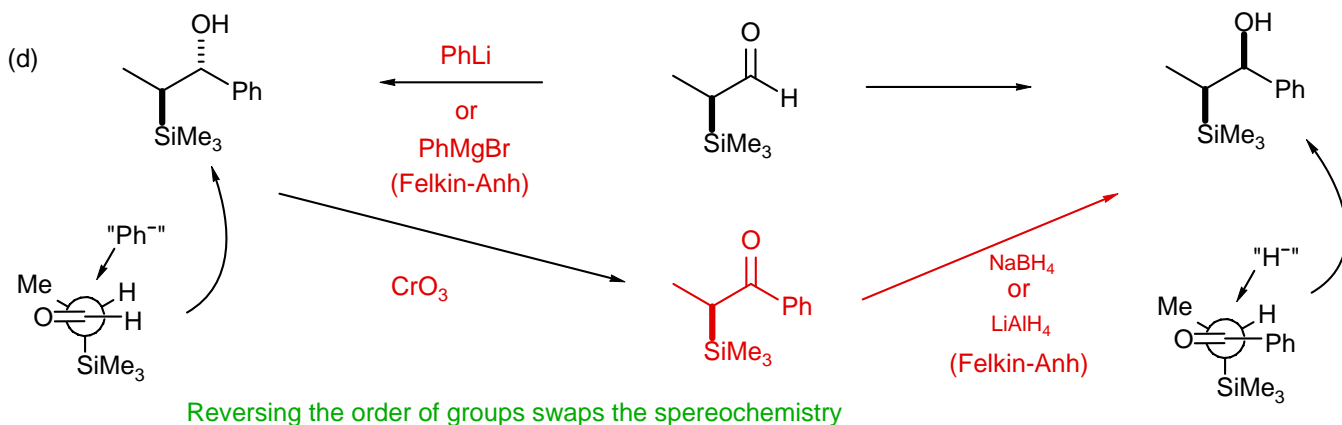Name **Grading**

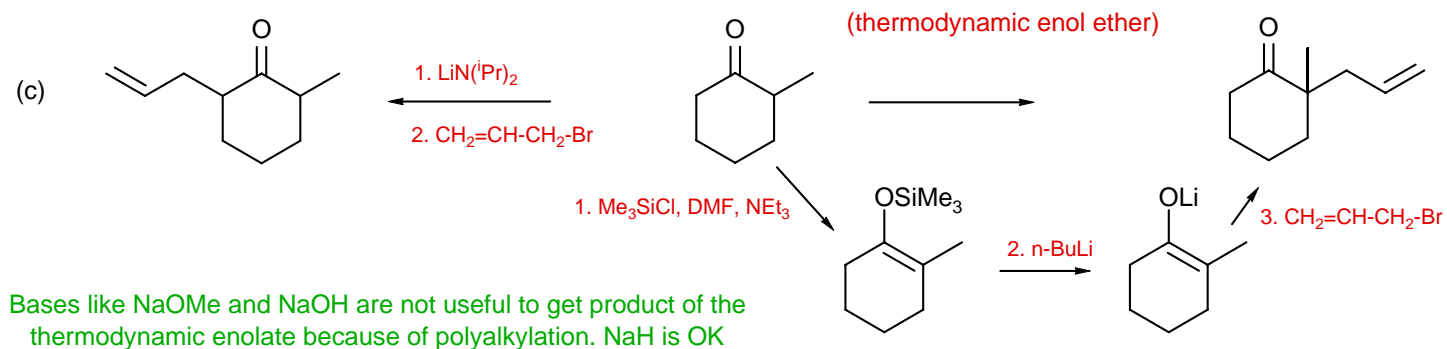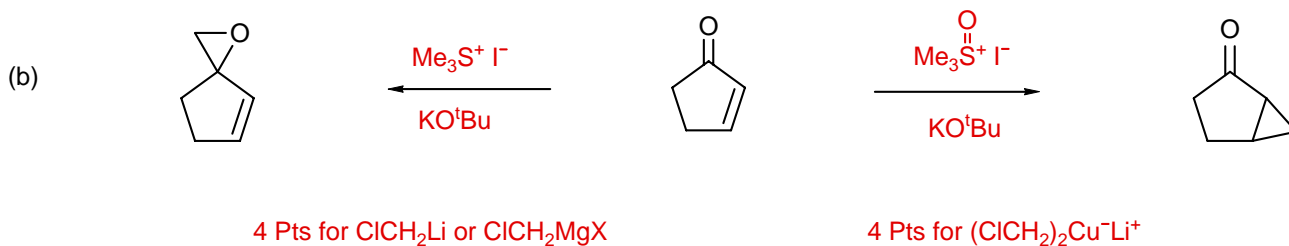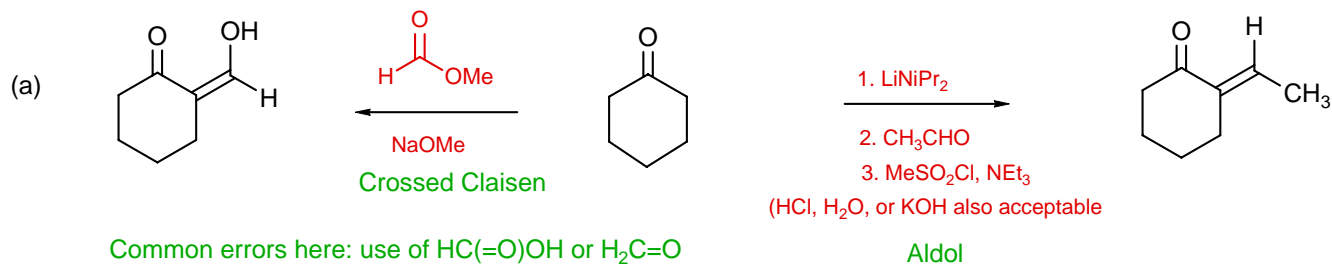Distribution from grade list (average: 64.1; count: 40)

If you place answers anywhere else except in the spaces provided,
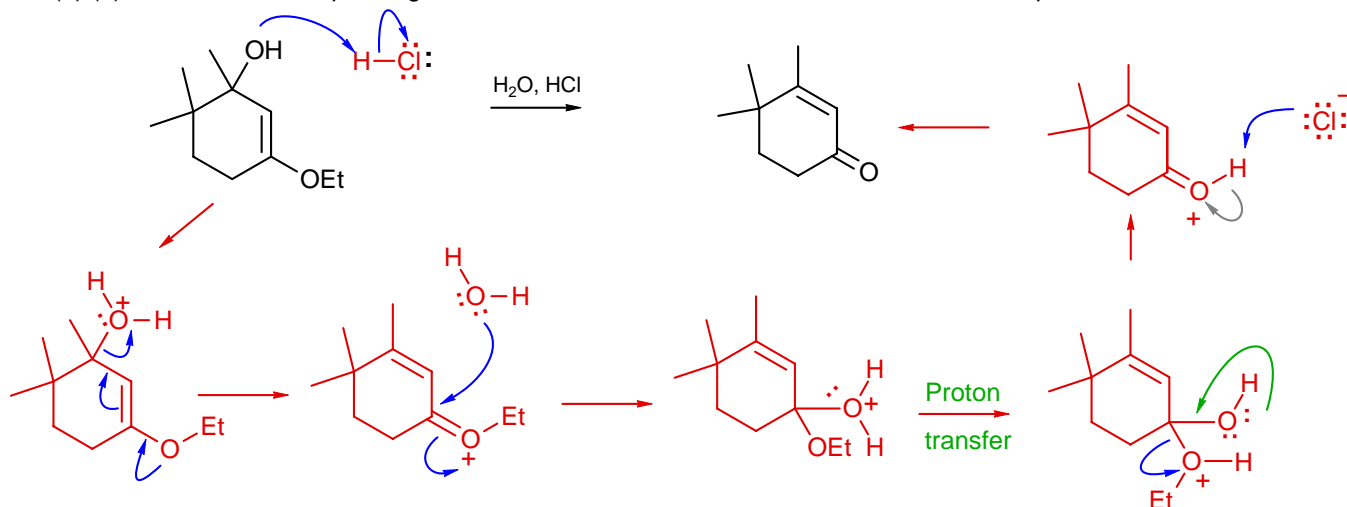clearly indicate this on the answer sheets.

NOTE: Do not use acronyms for reagents or solvents, unless you define them first.

For the synthetic transformations which involve more than one step, you should show the product of the reaction after each step, but you do not need to write mechanisms. Only question 2 requires detailed mechanisms.
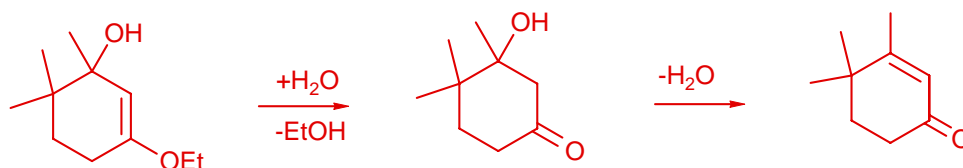
1. (32) Provide reagents and, if pertinent, reaction conditions, to accomplish the following selective transformations. If you use more than two steps show all intermediate products.

(a)

NaOMe

Crossed Claisen

Common errors here: use of HC(=O)OH or H₂C=O

1. LiNiPr₂
2. CH₃CHO
3. MeSO₂Cl, NEt₃
(HCl, H₂O, or KOH also acceptable

Aldol

·B

(b)

Me₃S⁺ I⁻

KOᵗBu

4 Pts for ClCH₂Li or ClCH₂MgX

Me₃S⁺ I⁻ (with O)

KOᵗBu

4 Pts for (ClCH₂)₂Cu⁻Li⁺

(c)

1. LiN(ⁱPr)₂
2. CH₂=CH-CH₂-Br

(thermodynamic enol ether)

1. Me₃SiCl, DMF, NEt₃

2. n-BuLi

3. CH₂=CH-CH₂-Br

Bases like NaOMe and NaOH are not useful to get product of the thermodynamic enolate because of polyalkylation. NaH is OK

(d)

PhLi
or
PhMgBr
(Felkin-Anh)

"Ph⁻"

CrO₃

NaBH₄
or
LiAlH₄
(Felkin-Anh)

"H⁻"

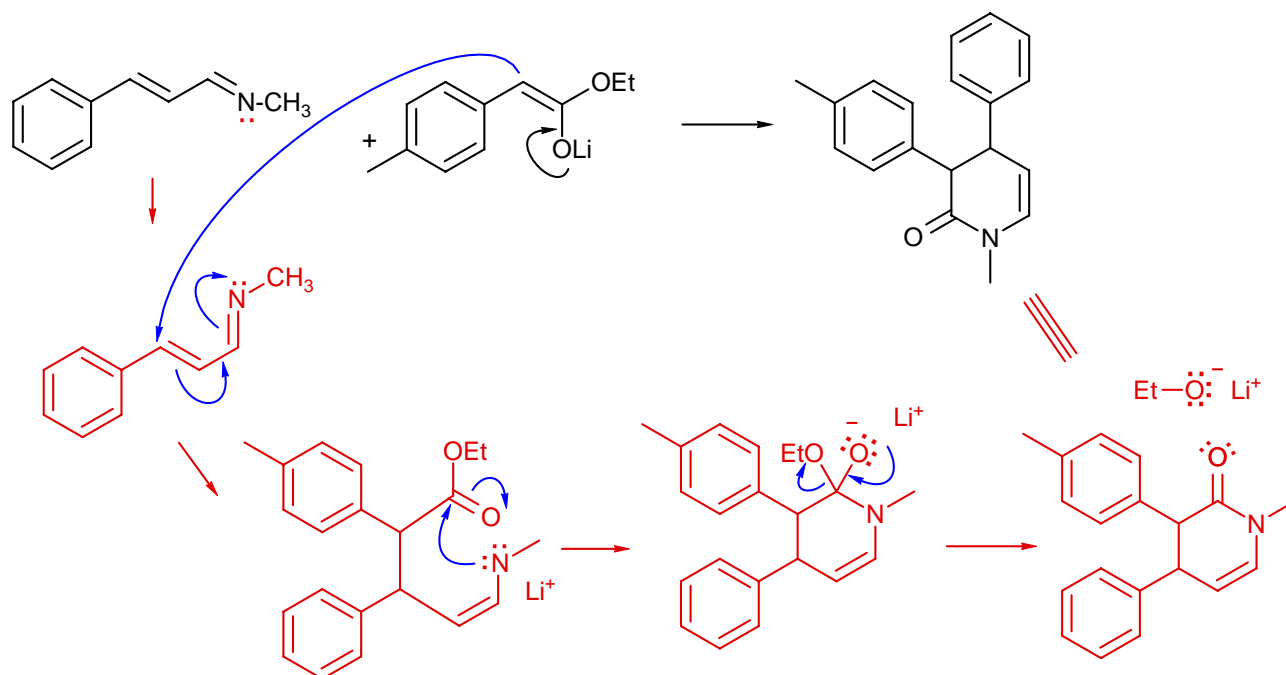Reversing the order of groups swaps the spereochemistry

2. (a) (8) Write an electron-pushing mechanism for the transformation below. Show all steps.
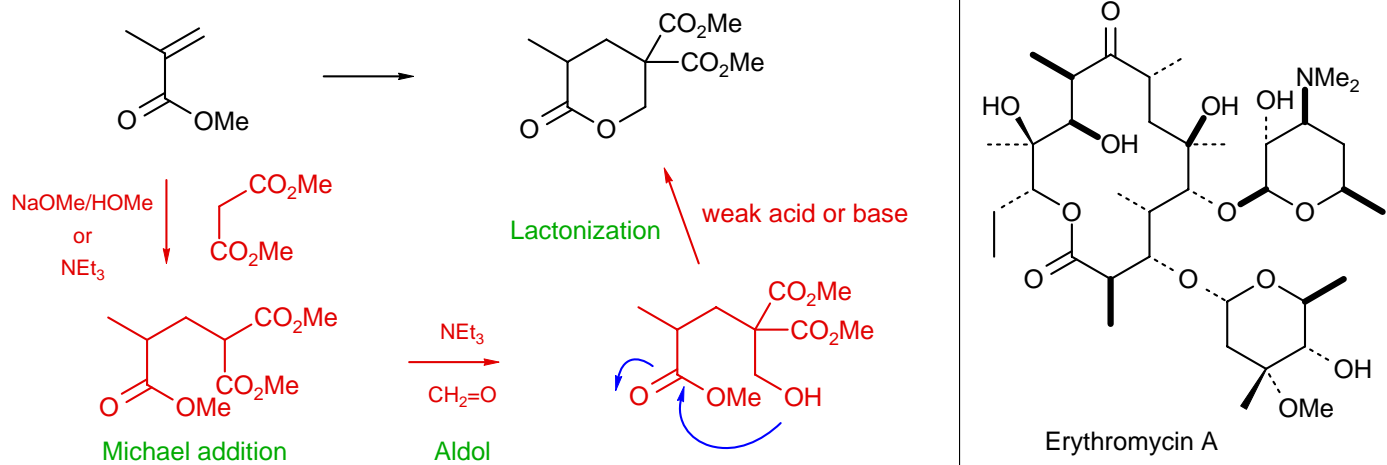

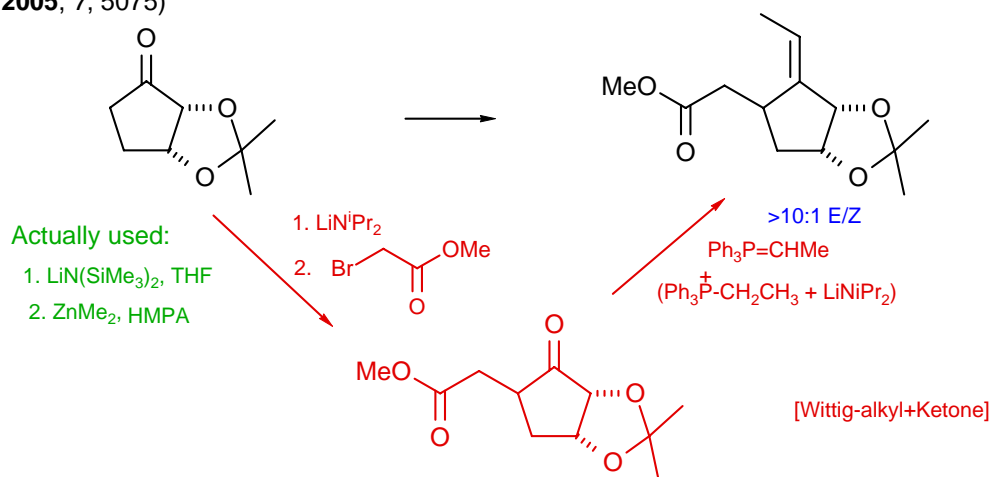Could also first hydrolyze the enol ether, then dehydrate:

(b) (8) Write an electron-pushing mechanism for the transformation below. Show all steps.
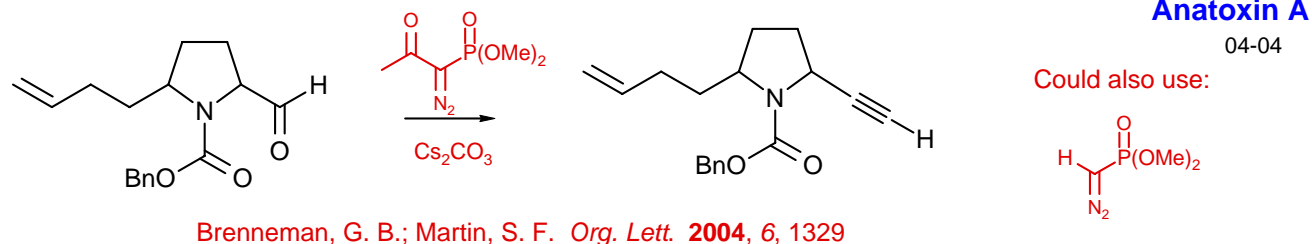
3. (a) (10) In the early part of a synthesis of Erythromycin A the following transformation was carried out. Show how this can be done.

NaOMe/HOMe or NEt₃

CO₂Me / CO₂Me

Michael addition

NEt₃
CH₂=O

Aldol

weak acid or base

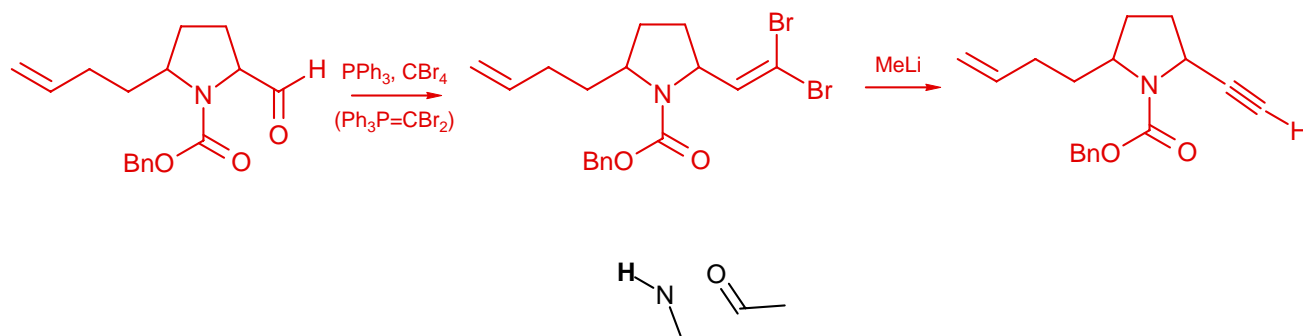Lactonization

Erythromycin A

(b) (10) Provide reagents and, if pertinent, reaction conditions, to accomplish the following transformation encountered in the synthesis of Oleocanthal (Smith, A. B.; Han, Q.; Breslin, P. A. S.; Beauchamp. G. K. *Org. Let.* **2005**, *7*, 5075)
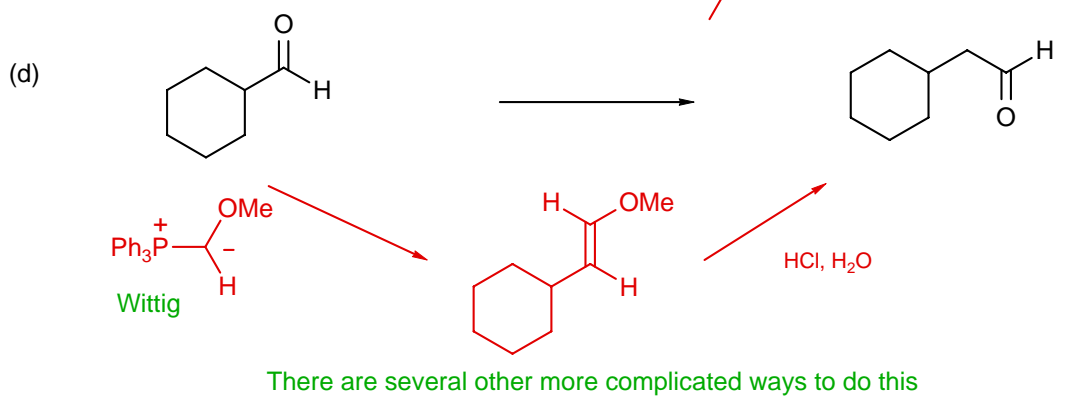

Actually used:
1. LiN(SiMe₃)₂, THF
2. ZnMe₂, HMPA

1. LiNⁱPr₂
2. Br—CH₂CO₂Me (OMe)

>10:1 E/Z
Ph₃P=CHMe
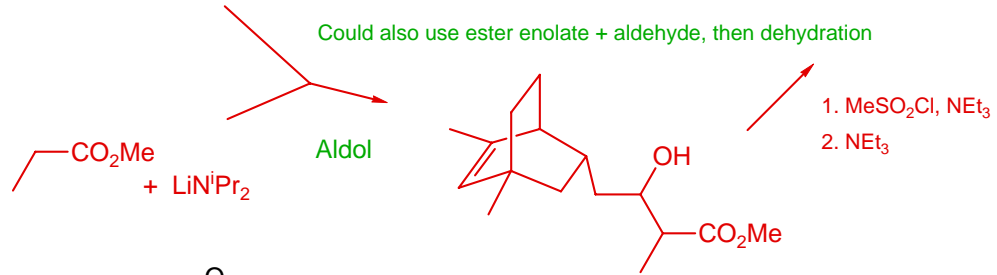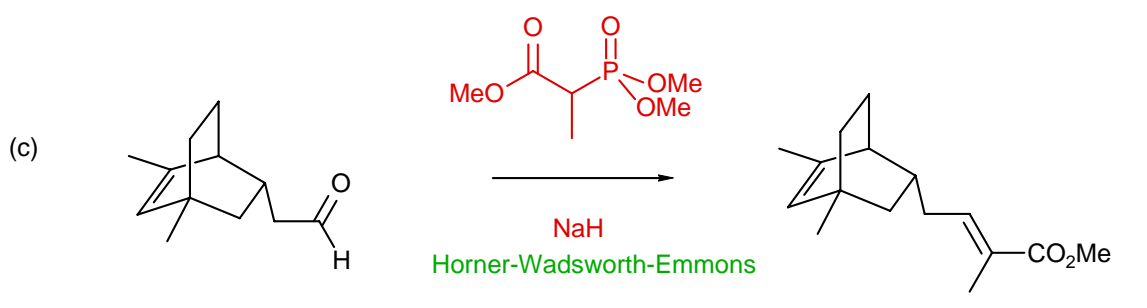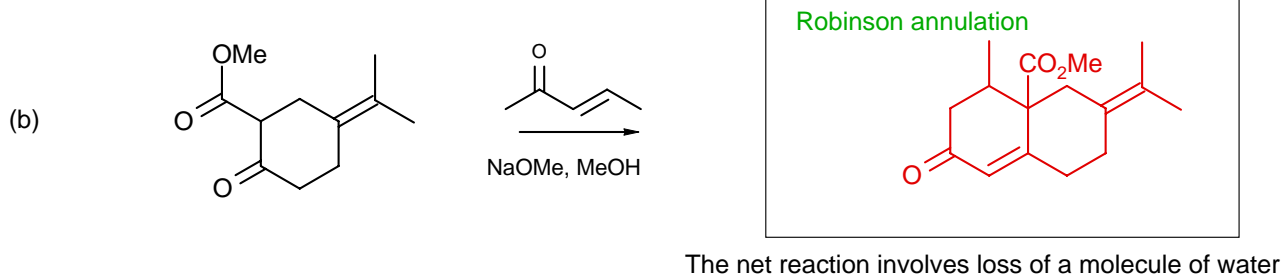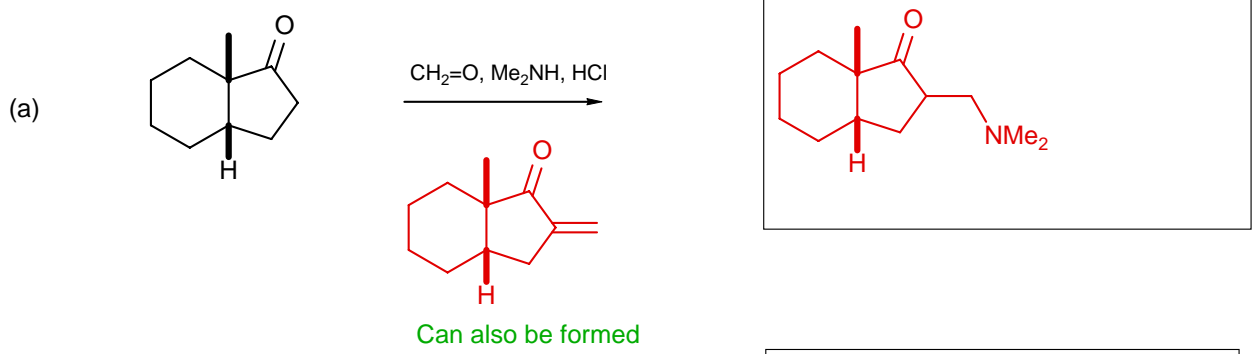(Ph₃P⁺-CH₂CH₃ + LiNiPr₂)

[Wittig-alkyl+Ketone]

(c) (5) In a 2004 synthesis of Anatoxin A the following transformation was carried out. Show how this can be done. Brenneman, G. B.; Martin, S. F. *Org. Lett.* **2004**, *6*, 1329

Anatoxin A
04-04

Cs₂CO₃

Brenneman, G. B.; Martin, S. F. *Org. Lett.* **2004**, *6*, 1329

Could also use:

H—P(OMe)₂ / N₂

or the Corey-Fuchs reaction, but there might be a potential problem with reactivity of the carbamate with MeLi
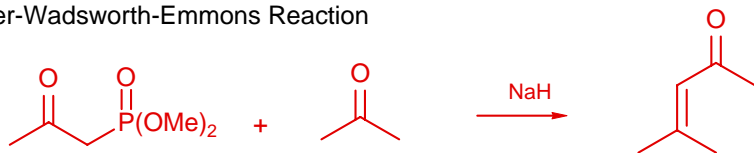

PPh₃, CBr₄
(Ph₃P=CBr₂)

MeLi

4. (20) Provide the missing product or reagents for the transformations below. You do not have to write mechanisms. For parts (c) and (d) write the product after each step if you use more than one step

(a)

CH$_2$=O, Me$_2$NH, HCl

Can also be formed

(b)

OMe

NaOMe, MeOH

Robinson annulation

CO$_2$Me

The net reaction involves loss of a molecule of water

(c)

MeO

P

OMe

OMe

NaH

Horner-Wadsworth-Emmons

CO$_2$Me

Could also use ester enolate + aldehyde, then dehydration

CO$_2$Me

+ LiN^{i}Pr$_2$

Aldol

OH

CO$_2$Me

1. MeSO$_2$Cl, NEt$_3$

2. NEt$_3$

(d)

O

H

H

OMe

Ph$_3$P

H

Wittig

H

OMe

H

HCl, H$_2$O

H

O

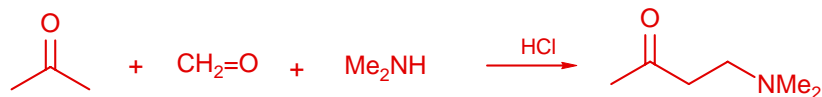There are several other more complicated ways to do this

5. (7) The following name reactions have been discussed in the course. Give a specific (no "R" or "X" groups) example of two of them. Identify which you have chosen!
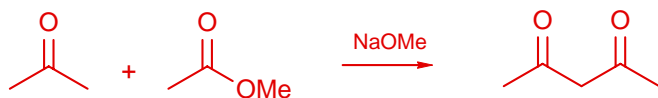
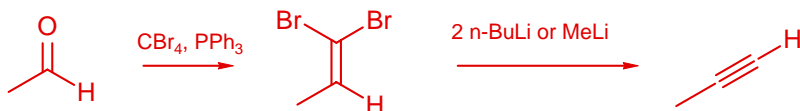Horner-Wadsworth-Emmons Reaction
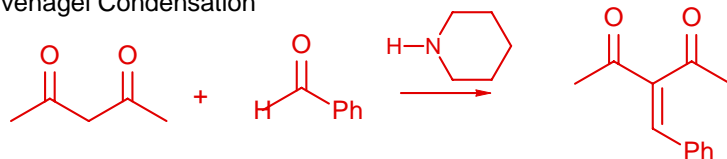

Mannich Reaction

Claisen Condensation

Corey-Fuchs Reaction

Koevenagel Condensation

Morita-Bayliss-Hillman Reaction