STRATEGIES IN SYNTHESIS

Professor T. J. Donohoe

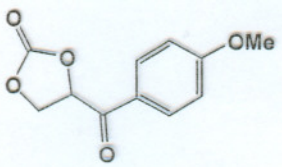
MT 2007

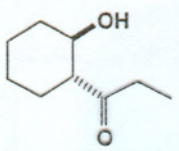
6 Lectures: Tuesday at 10 am; Thursday at 9 am (weeks 6-8)

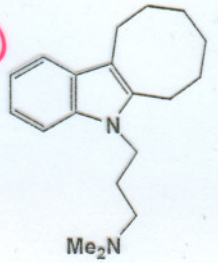
ANSWERS TO QUESTIONS

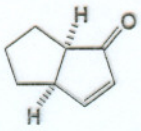
Some problems to think about:

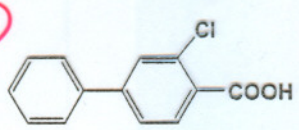
Disconnect the following and then devise forward syntheses:

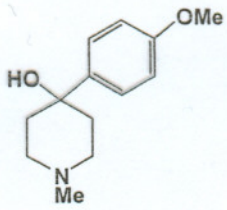
1 

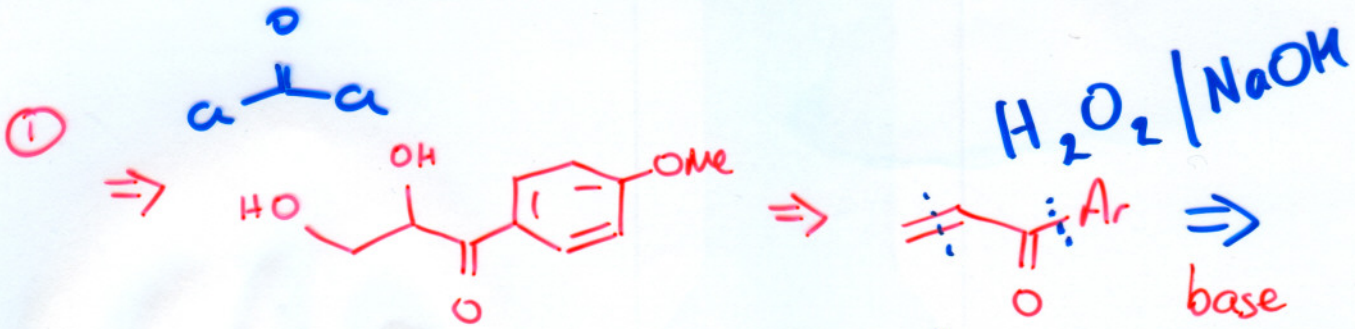
2 

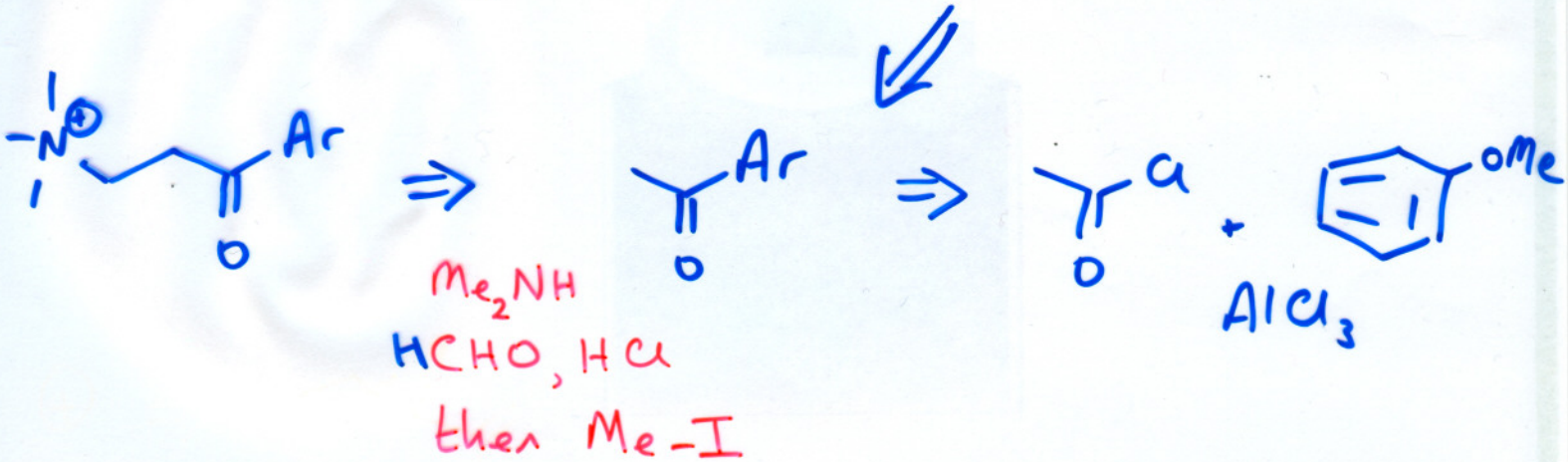
3 

4 

5 

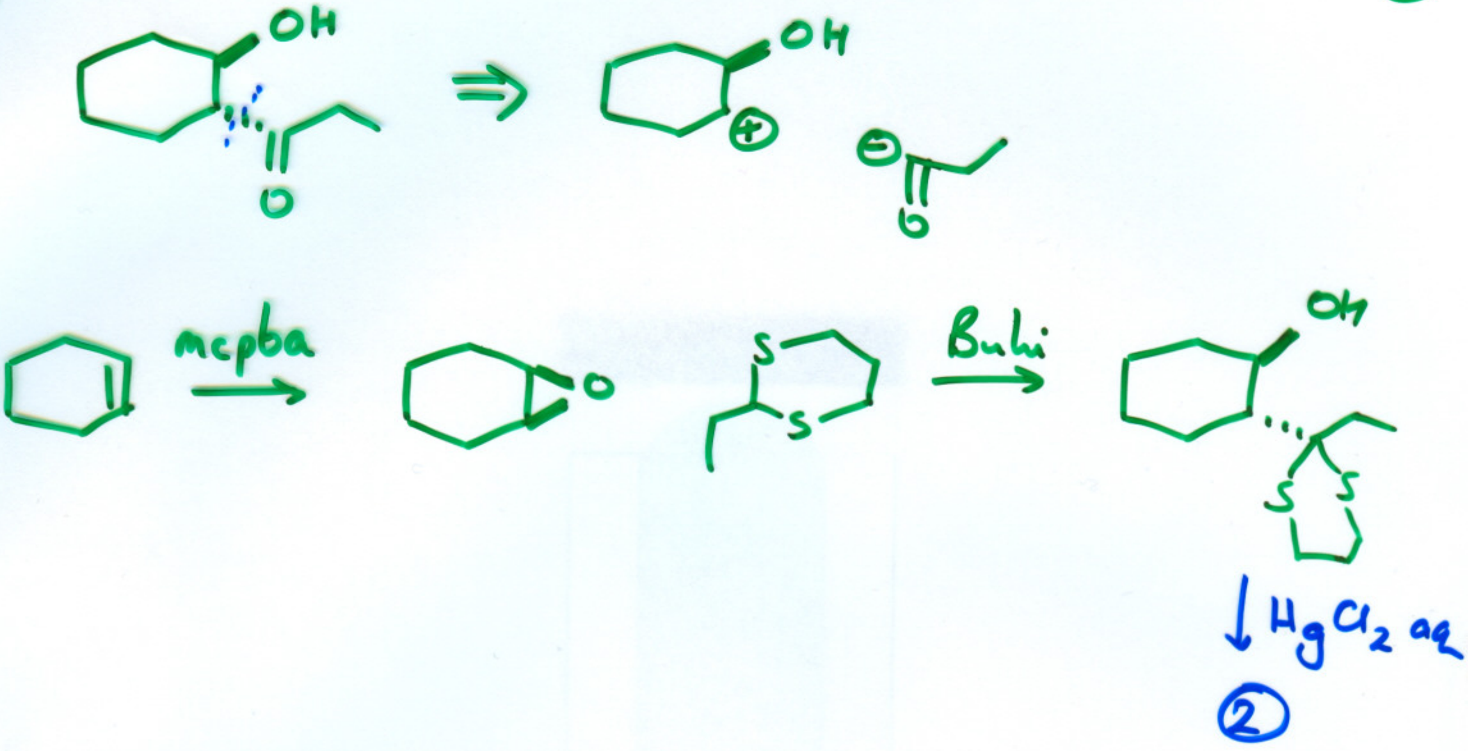
6 

1 



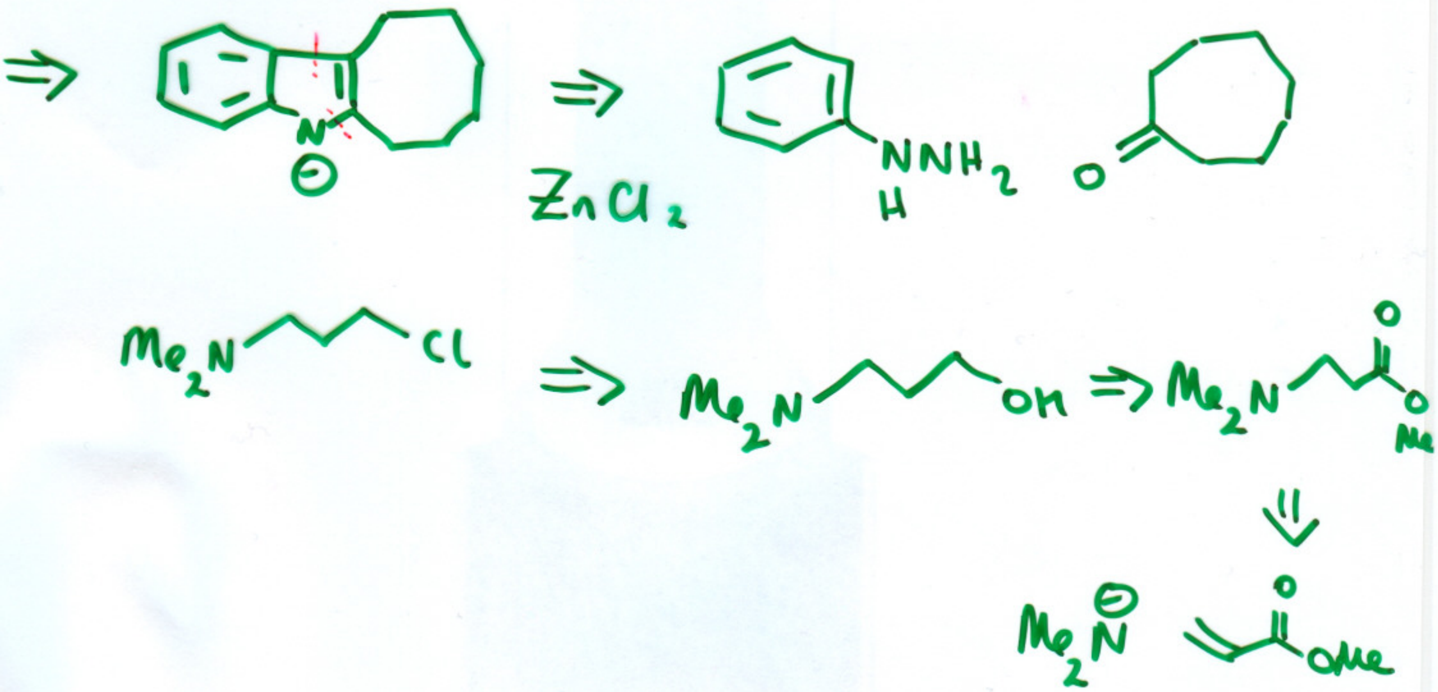
(2)

(2)



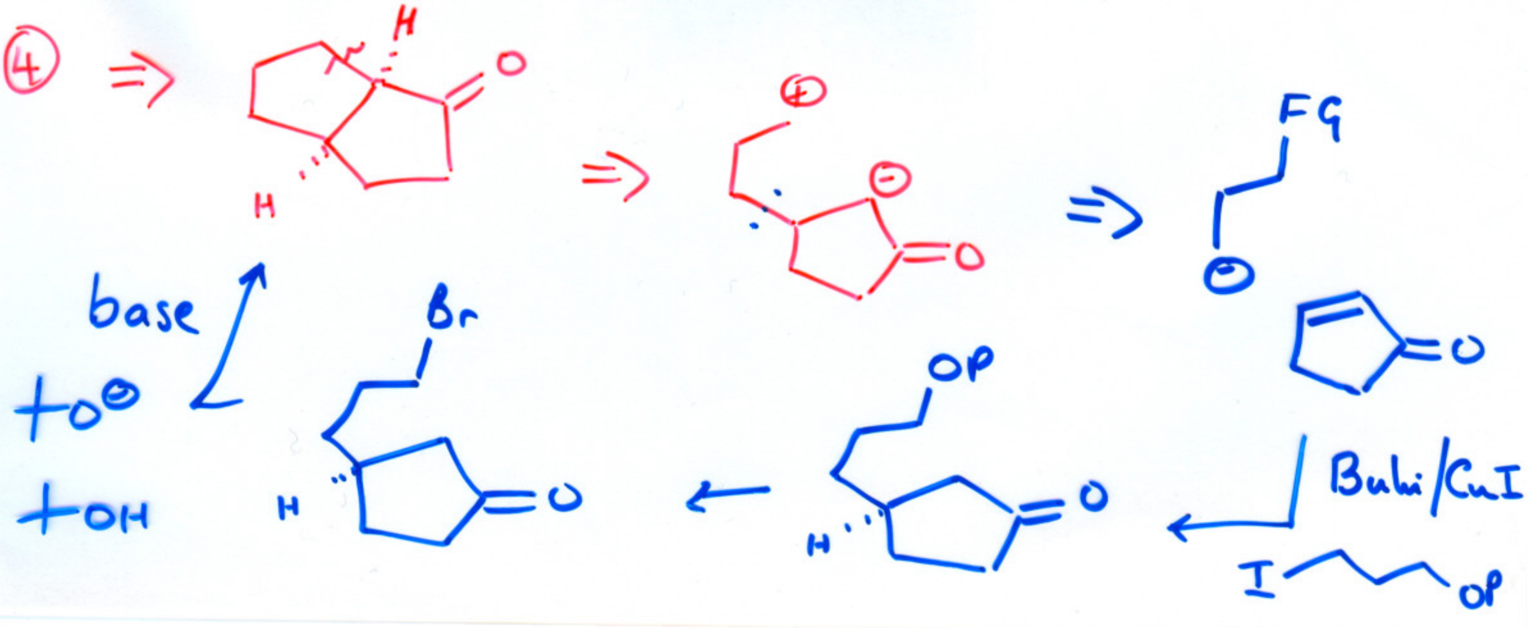
OH
OH
OH
mcpba
O
BuLi
HgCl2 aq
(2)

(3)

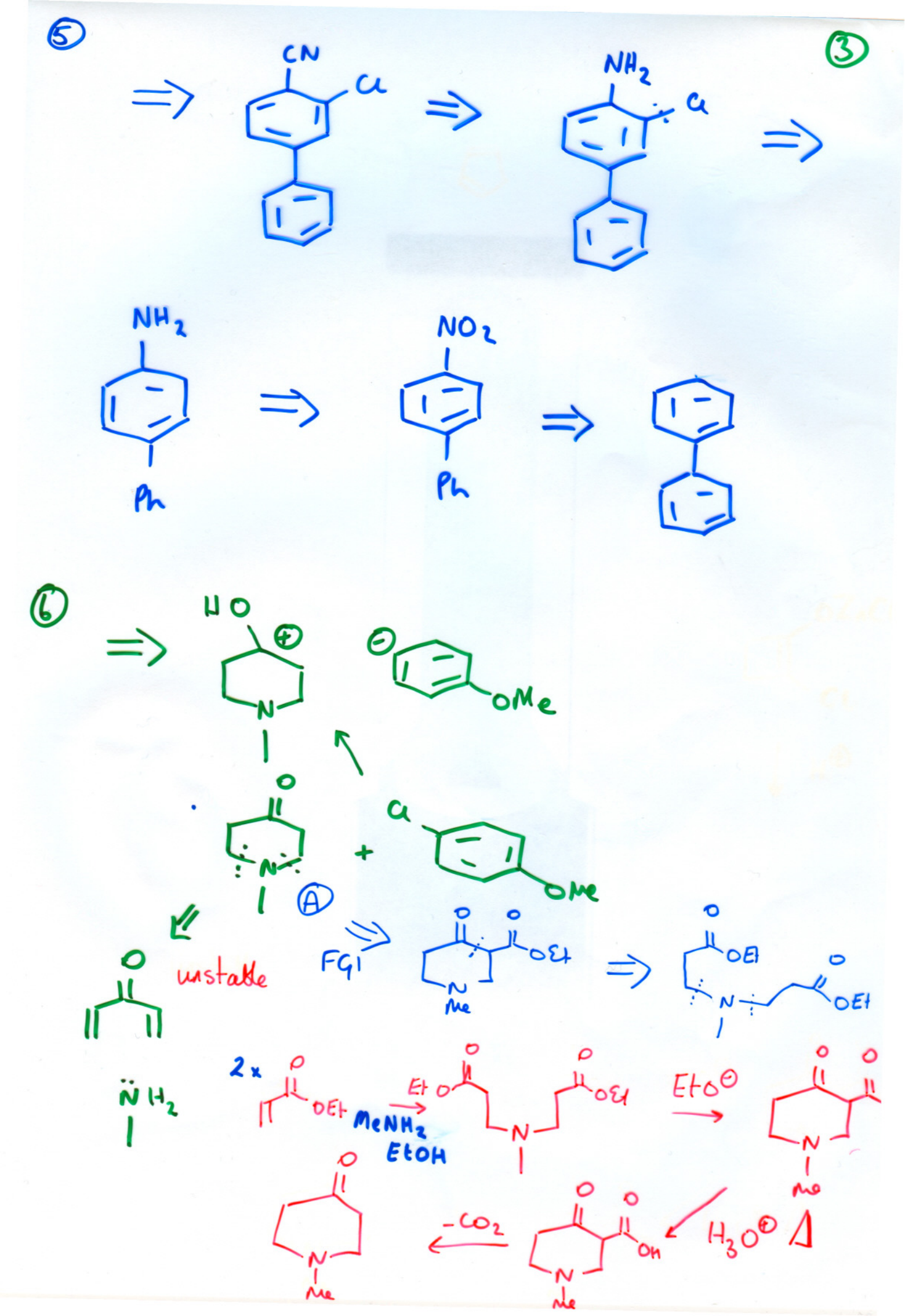


N
ZnCl2
NNH2
H
O
Me2N
Cl
Me2N
OH
Me2N
O
OMe
Me2N
O
OMe

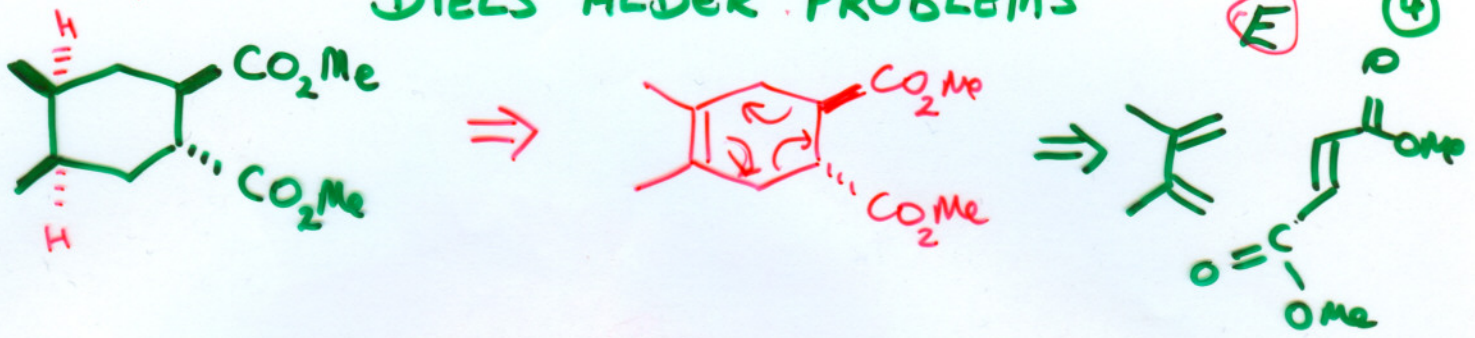
(4)

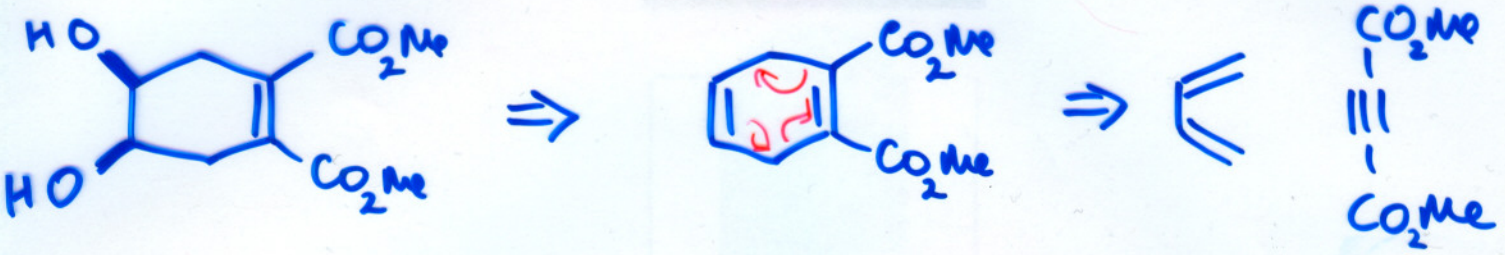


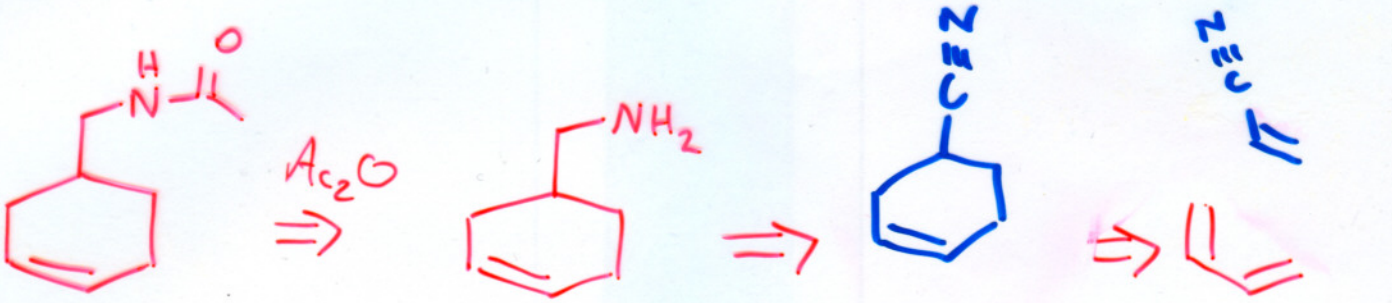
H
O
H
FG
O
base
Br
OP
+O⊖
+OH
H
O
H
O
BuLi/CuI
I
OP

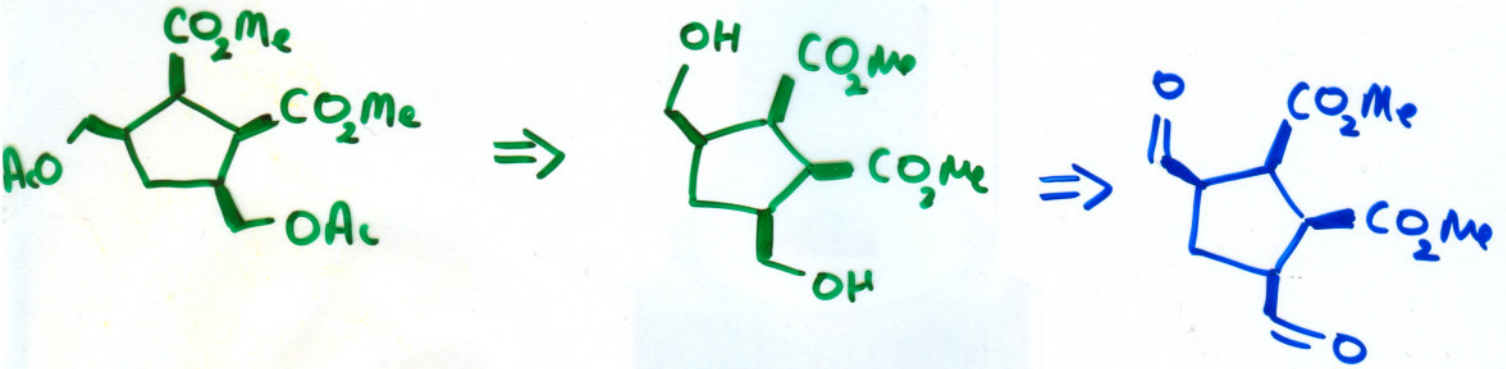

5
CN
Cl
3
NH2
Cl
NH2
Ph
NO2
Ph
6
HO
N
OMe
O
N
A
Cl
+
OMe
unstable
FGI
O
OEt
N
Me
OEt
O
N
OEt
2 x
NH2
OEt
MeNH2
EtOH
Et O
OEt
N
EtO⊖
N
Me
N
Me
-CO2
OH
N
Me
H3O⊕ Δ

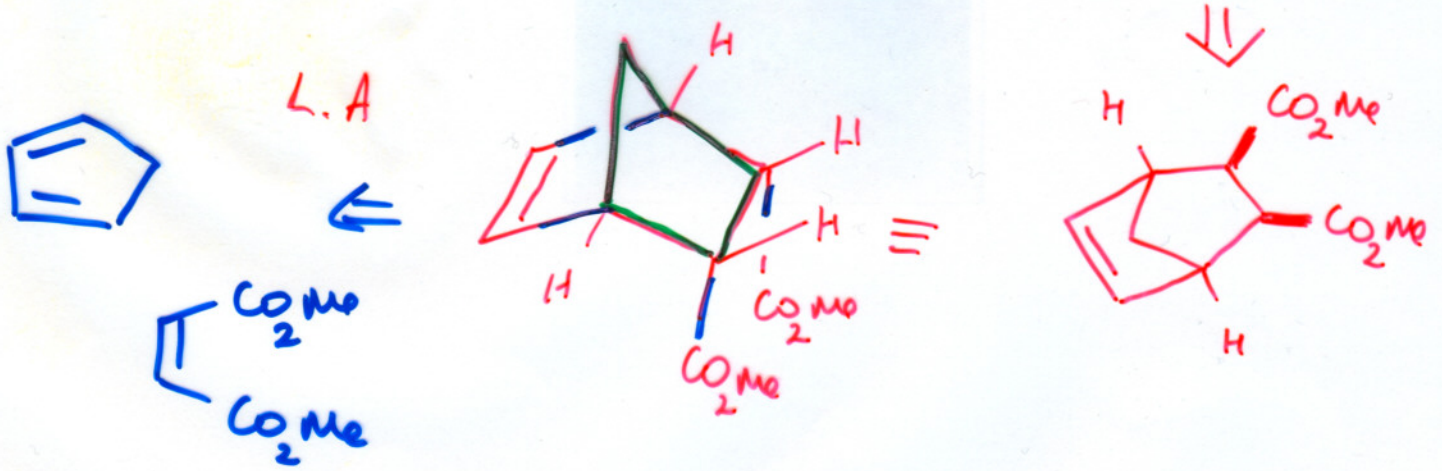
DIELS ALDER PROBLEMS











PAST PAPER

5

1. Answer *both* Parts **A** and **B**.

Part A.

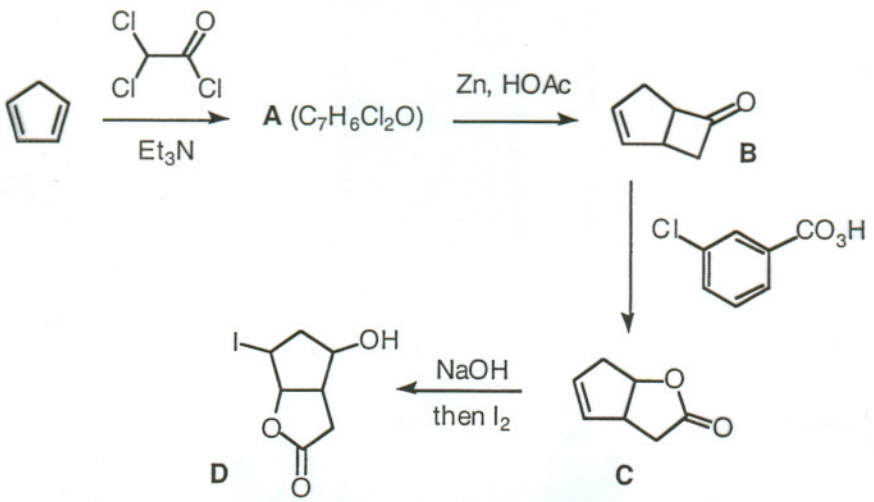
The following sequence was used in a synthesis of prostaglandin PGA_2.

(a) What is the structure and relative stereochemistry of **A**? Draw a mechanism to explain its formation. [4]

(b) Give a mechanism for the conversion of **A** into **B**. [3]

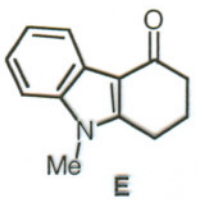
(c) Give a mechanism for the conversion of **B** into **C**. Explain the regiochemistry of this reaction. [4]

(d) Draw mechanisms for the conversion of **C** into **D** and predict the relative stereochemistry of **D**. [4]



Part B.

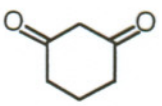
Devise a synthesis for compound **E** from the starting materials indicated, and other reagents of your choice. Show mechanisms for the reactions involved in your synthesis. [5]



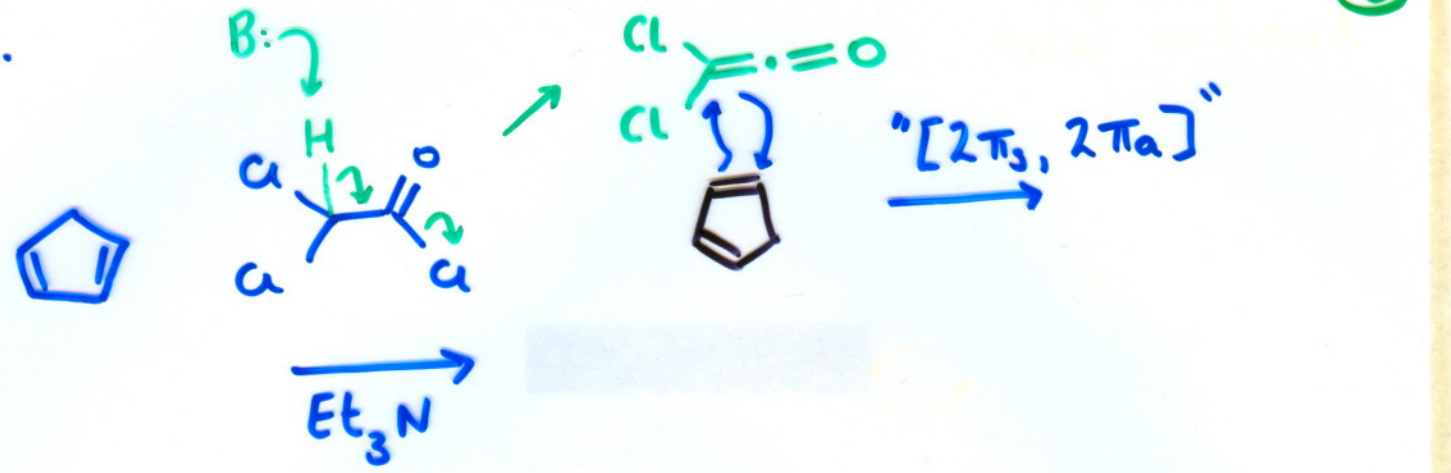
E

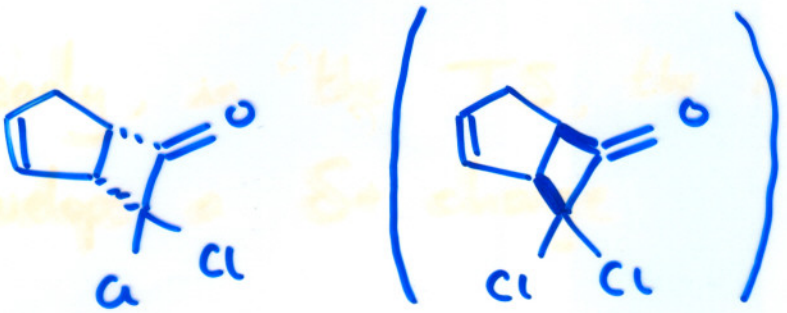
starting materials

$PhNHNH_2$



Q1.





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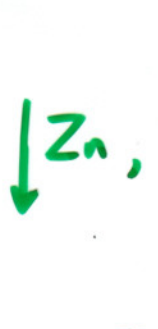
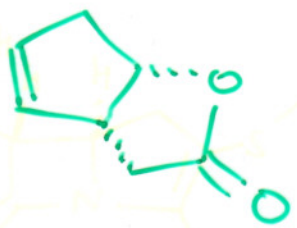
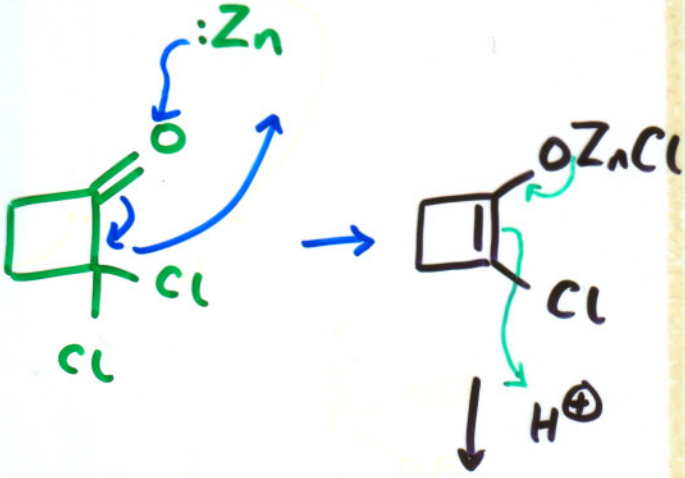
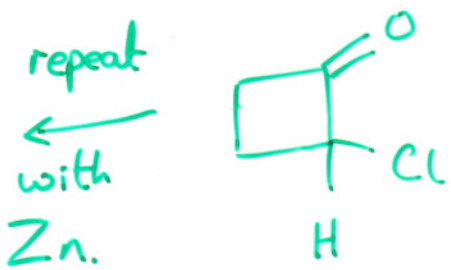








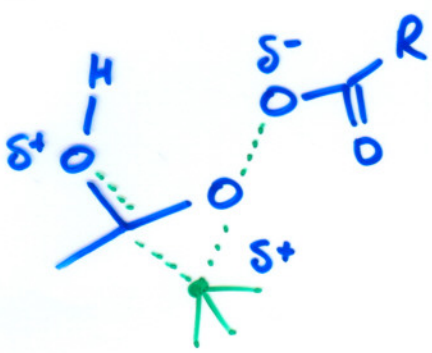
standard Baeyer-Villiger mechanism. (see estradiol)

2 points of interest.

(A) regiochemistry. The group that migrates is that best able to stabilise a positive charge. i.e.

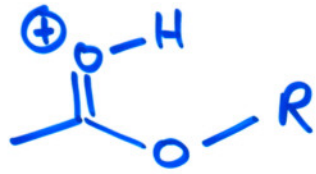
$^{t}Bu > {}^{s}Bu \sim Ar > {}^{n}Bu > Me$

clearly, in the T.S. the migrating group develops a δ+ charge



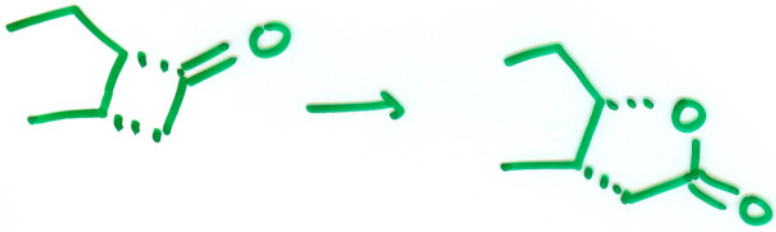
$T^{\neq}$

remember the product is



ie it bears a full positive charge; some of this is reflected in the T.S leading to it.

(B) Stereochemistry. RETENTION during migration



d) C-D iodolactonisation.

Identical mech to that shown in $PGF_{2\alpha}$

B) Fisher indole