Chemistry 3B, Final Examination

Monday, December 16, 2002

Student name: Answer Key

Student signature: _____

Write TA's name or Lecture Only: _____

1. Please make sure that the exam has 15 pages including this one.
2. Please write your answers in the spaces provided.
3. Write clearly; illegible or ambiguous answers will be considered incorrect.
4. Only writing implements are allowed **(No Calculators)**.

GOOD LUCK!

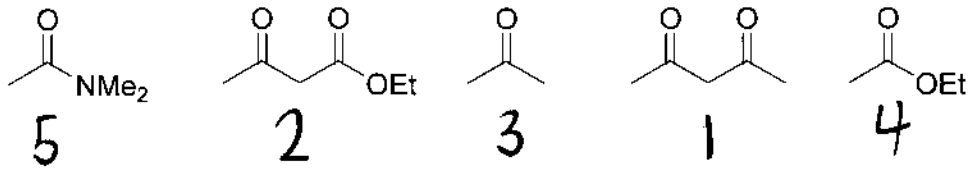
1.	40 points	_____
2.	60 points	_____
3.	60 points	_____
4.	25 points	_____
5.	25 points	_____
6.	30 points	_____
7.	30 points	_____
8.	30 points	_____
9.	30 points	_____
10.	15 points	_____
11.	15 points	_____
Total	**360 points**	_____

MINI-PERIODIC TABLE

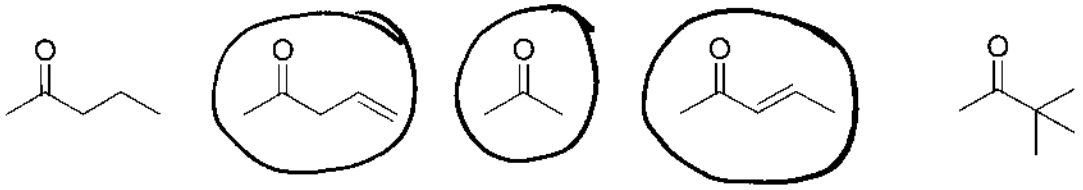
I	II	III	IV	V	VI	VII	VIII
H							He
Li	Be	B	C	N	O	F	Ne
Na	Mg	Al	Si	P	S	Cl	Ar
K	Ca	Ga	Ge	As	Se	Br	Kr

1. Answer the following questions. Every wrong answer cancels a correct answer (40 points total).

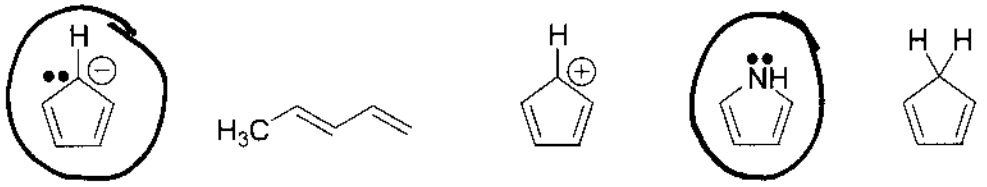
(a). Rank the structures from most acidic to least acidic [1 = **most** acidic, 5 = **least** acidic] (8 points).



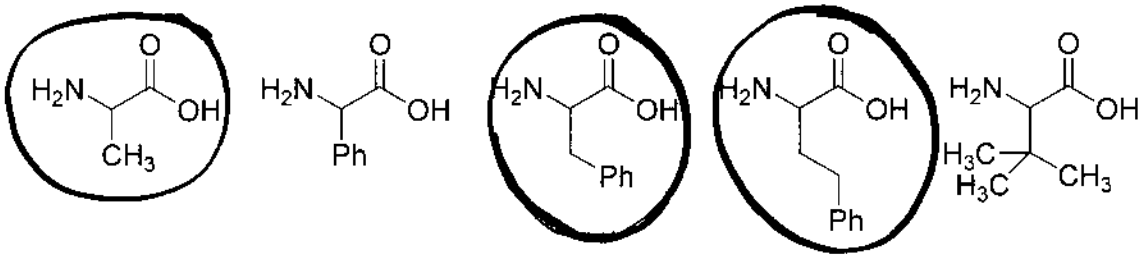
(b). Circle the compounds that upon treatment with D_3O+ incorporate ≥ 6 deuteriums (8 points).



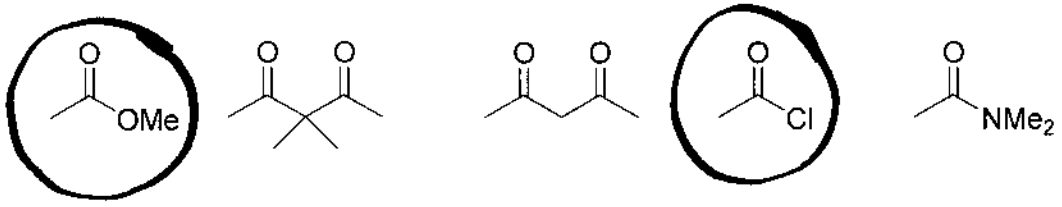
(c). Circle the compounds that are aromatic (8 points).



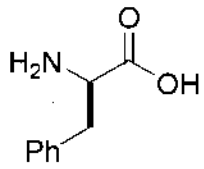
(d). Circle the amino acids that could be synthesized by the Gabriel amino acid synthesis method, i.e., starting with $(EtO_2C)_2CHNPhth$ (8 points).



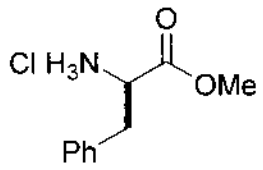
(e). Circle the compounds that give an ethyl ester as one of the products upon reaction with EtO-, EtOH, Δ (8 points).

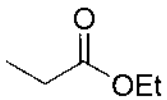


2. For each of the following reactions supply the missing reagents or major organic product in the space provided. If no reaction is expected indicate by N.R. (60 points total, 4 points each question).

(a) 

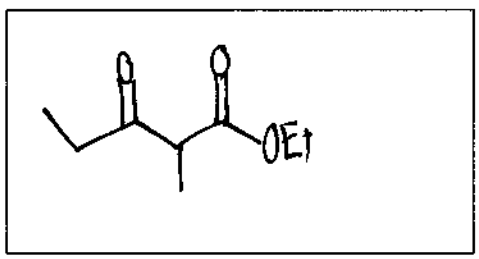
1. MeOH, HCl, Δ

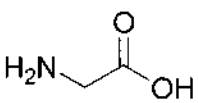


(b) 

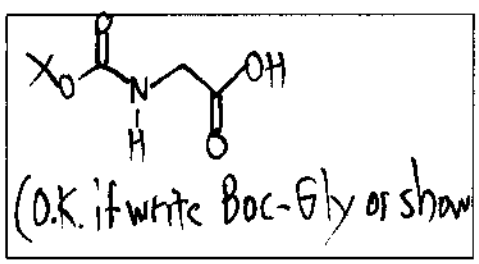
NaOEt (>0.5 equiv), EtOH

then aq. work-up

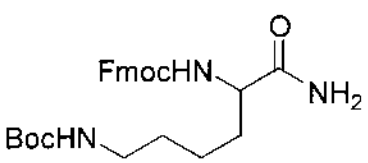


(c) 

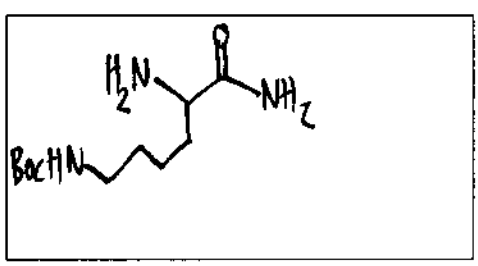
NaOH (1 equiv),
H_2O,
$(t\text{-}BuO_2C)_2O$

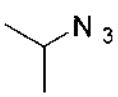


(O.K. if write Boc-Gly or show carbox.)

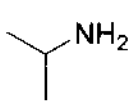
(d) 

piperidine

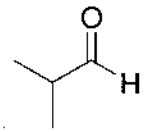


(e) 

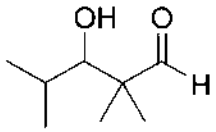
1. $LiAlH_4$, then aqueous workup



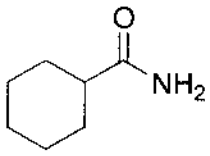
(f)



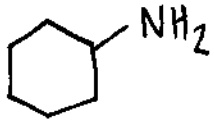
1. $NaOH, H_2O$ (no Δ)



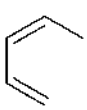
(g)



$NaOH, H_2O, Cl_2$



(h)



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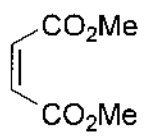
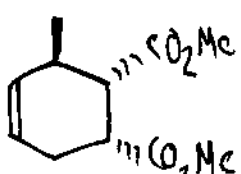
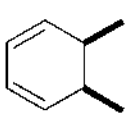


Δ

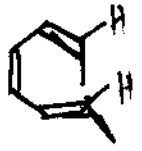


either enantiomer O.K.

(i)

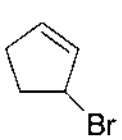


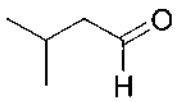
hv

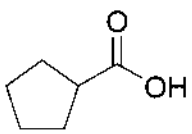


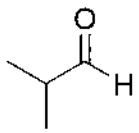
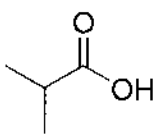
(j)

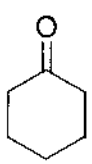
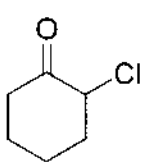
1. hv, NBS, CCl_4

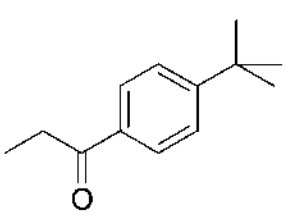
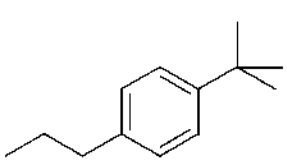


(k)  $NaOH, H_2O, \Delta$ → either isomer O.K.

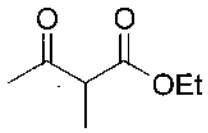
(l)  $LiAlH_4$, then aqueous work-up →

(m)  1. CrO_3, H_2O, H_2SO_4 → 

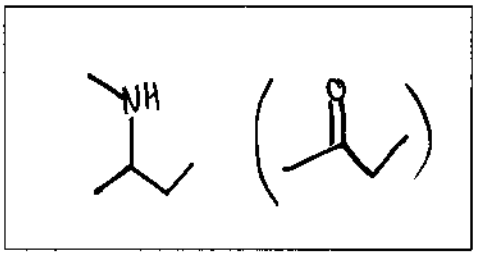
(n)  1. Cl_2, AcOH → 

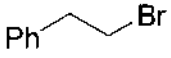
(o)  1. $H_2N\text{-}NH_2, \overset{\ominus}{O}H, \Delta$ → 

3. For each of the following reactions supply the missing reagents or major organic product in the space provided. If no reaction is expected indicate by N.R. (60 points total, 6 points each question).

(a) 

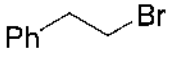
1. H_3O+, H_2O, Δ
2. $MeNH_2$, EtOH, $NaBH_3CN$

→ 

(b) 

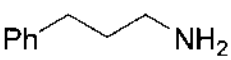
1. NaN_3
2. $LiAlH_4$, then aqueous work-up

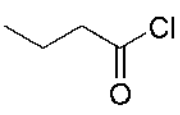
→ 

(c) 

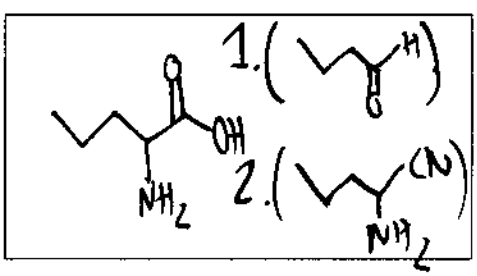
1. $NaCN$
2. $LiAlH_4$, then aqueous work-up

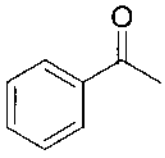
→ 



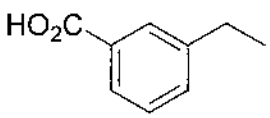
(d) 

1. $LiAl[OCH(CH_3)_3]_3$ then aqueous work-up
2. HCN, NH_3
3. H_3O+, H_2O, Δ

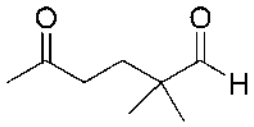
→ 

(e) 

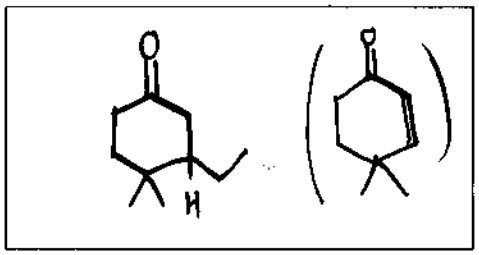
1. Br_2, $FeBr_3$
2. H_2NNH_2, $^{\ominus}OH$, Δ
3. Mg
4. CO_2 then aqueous work-up

→ 

(f)



1. $NaOH$, H_2O, Δ
2. Et_2CuLi, then aqueous work-up



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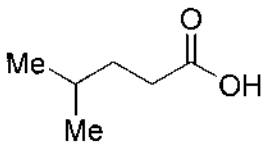
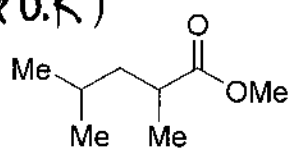
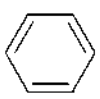
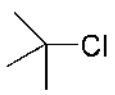


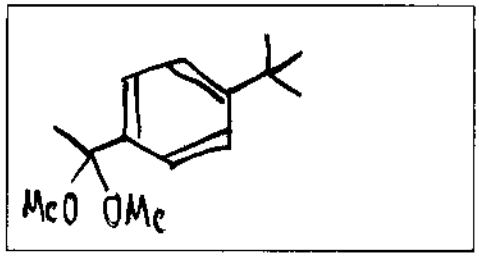
1. MeOH, $H^{\oplus}$ ($SOCl_2$ then MeOH would be O.K.)
2. LDA (CH_2N_2 would be O.K.)
3. MeI



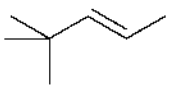
(h)



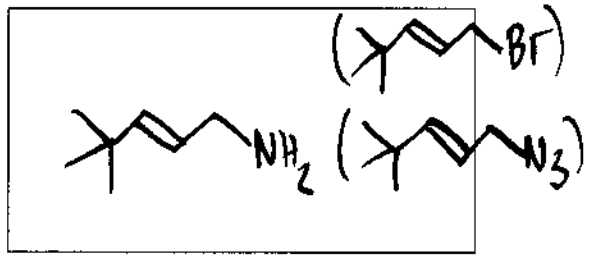
1. $AlCl_3$, 
2. $AlCl_3$  aqueous work-up
3. MeOH, HCl, sieves



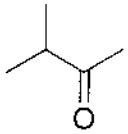
(i)



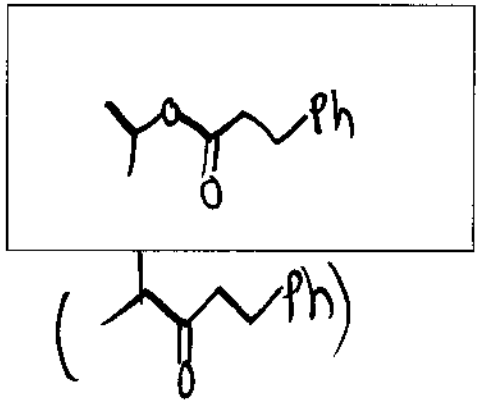
1. NBS, hv, CCl_4
2. NaN_3
3. $LiAlH_4$, aq. work-up



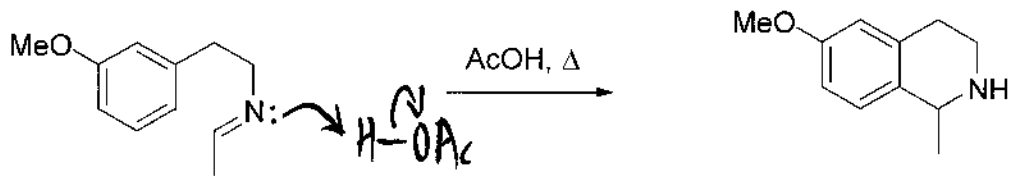
(j)



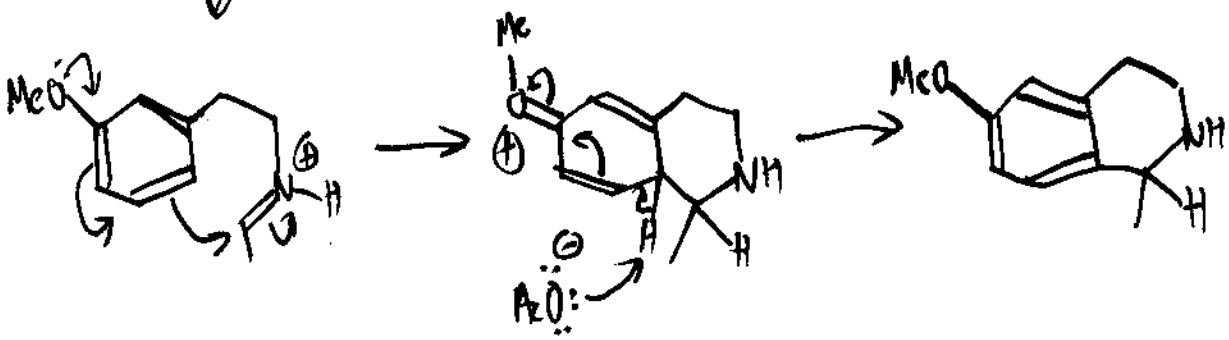
1. LDA
2. $PhCH_2Br$
3. F_3CCO_3H



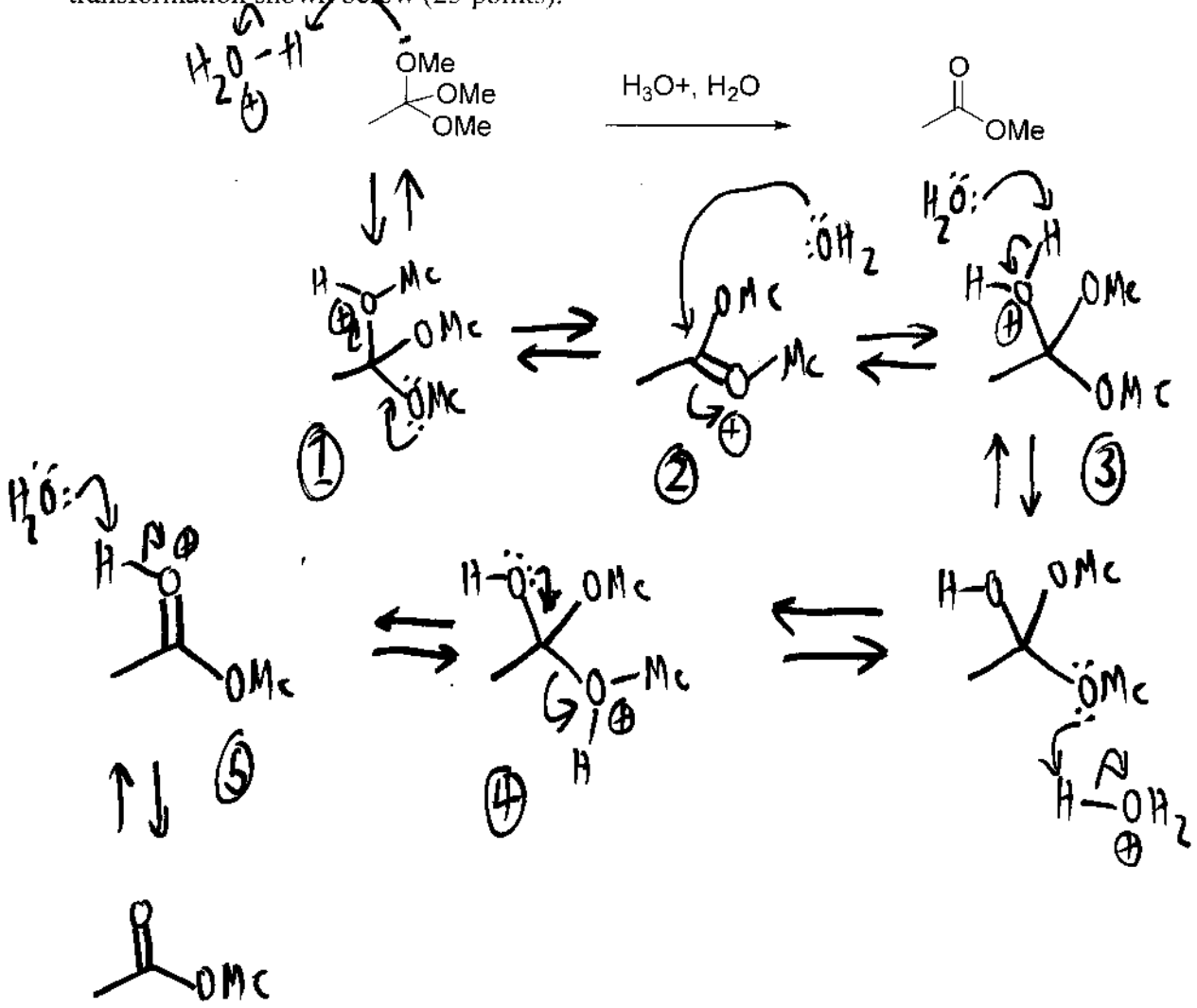
4. Provide a mechanism for the below transformation (25 points).



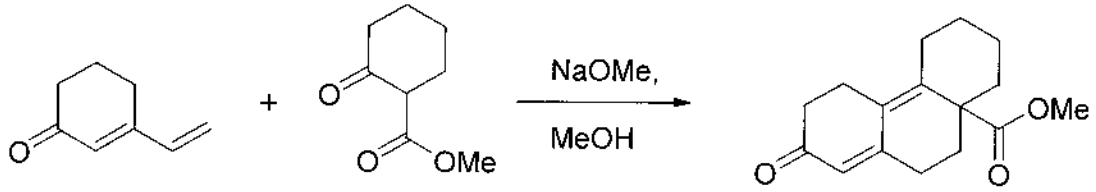
This type of reaction is called the Pictet Spengler reaction and can be used to synthesize morphine, vicodin and related compounds

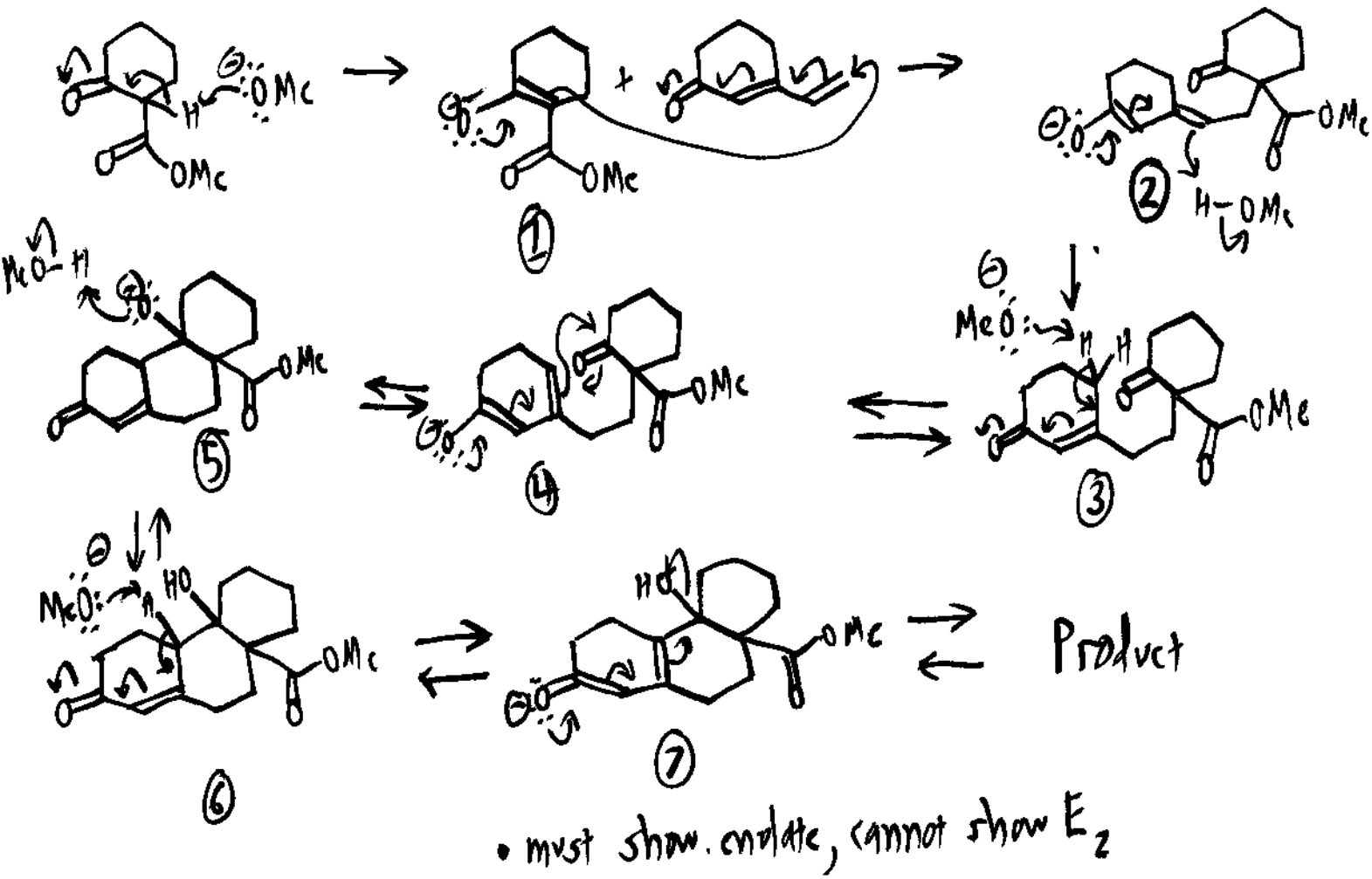


5. Orthoesters are used as protecting groups for esters. Provide a mechanism for the orthoester to ester transformation shown below (25 points).



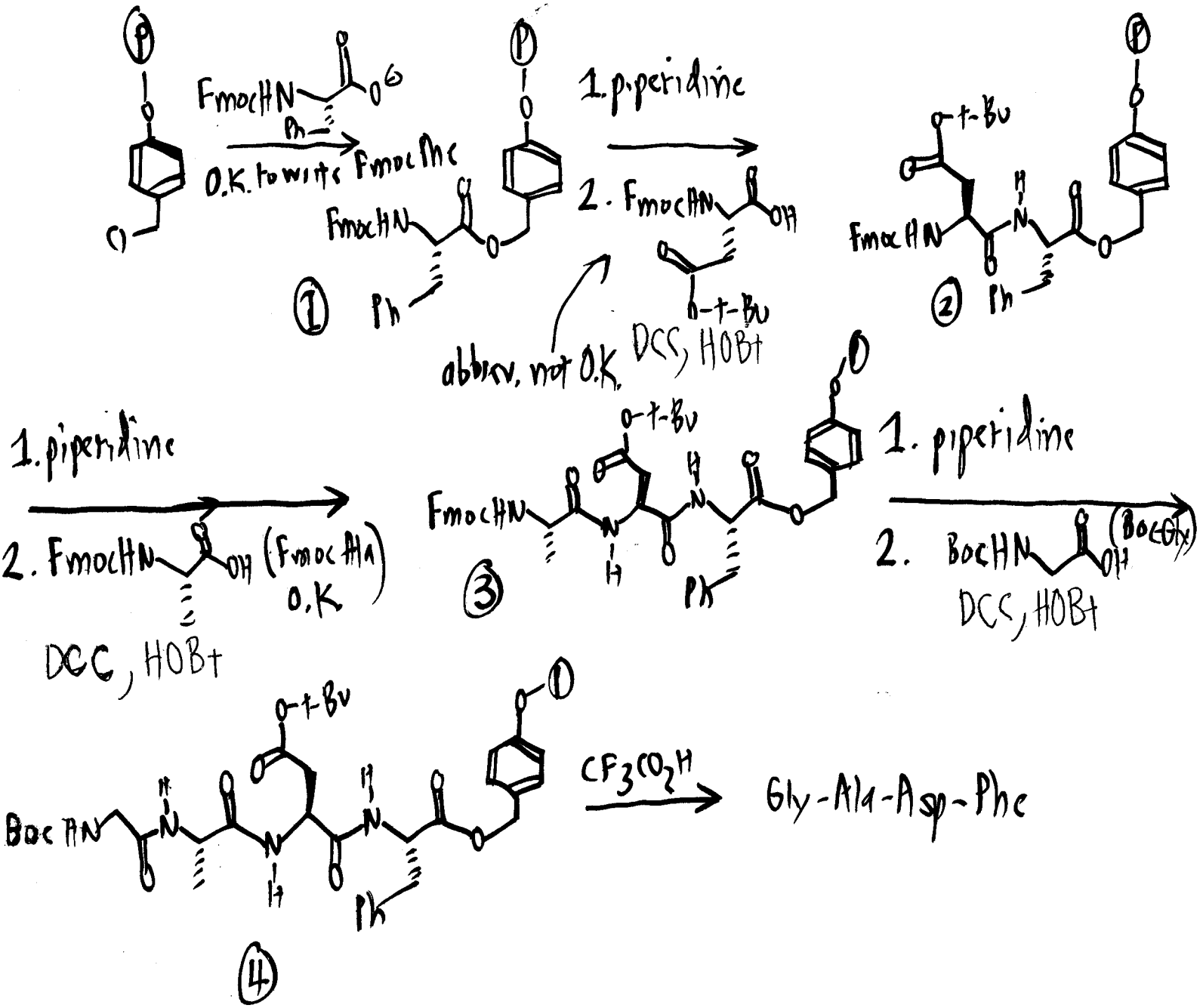
6. Provide a mechanism for the below transformation. **Hint:** think about the relationship of the below transformation to the Robinson annulation (30 points).



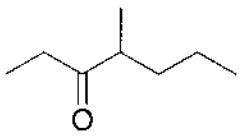


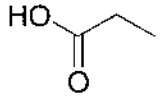
- must show. mechanism, cannot show E_2

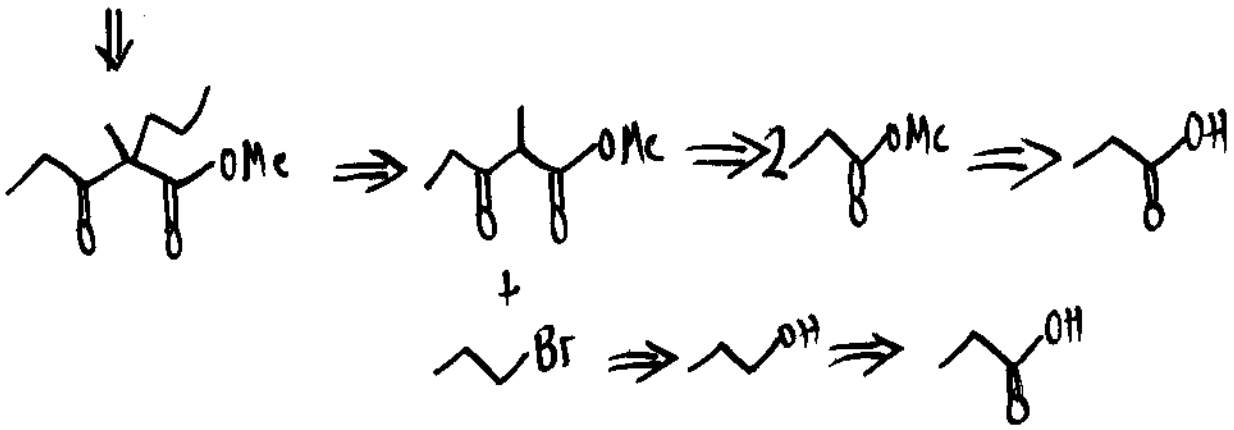
7. Provide the most efficient solid-phase synthesis of Gly-Ala-Asp-Phe from any protected amino acids (30 points).



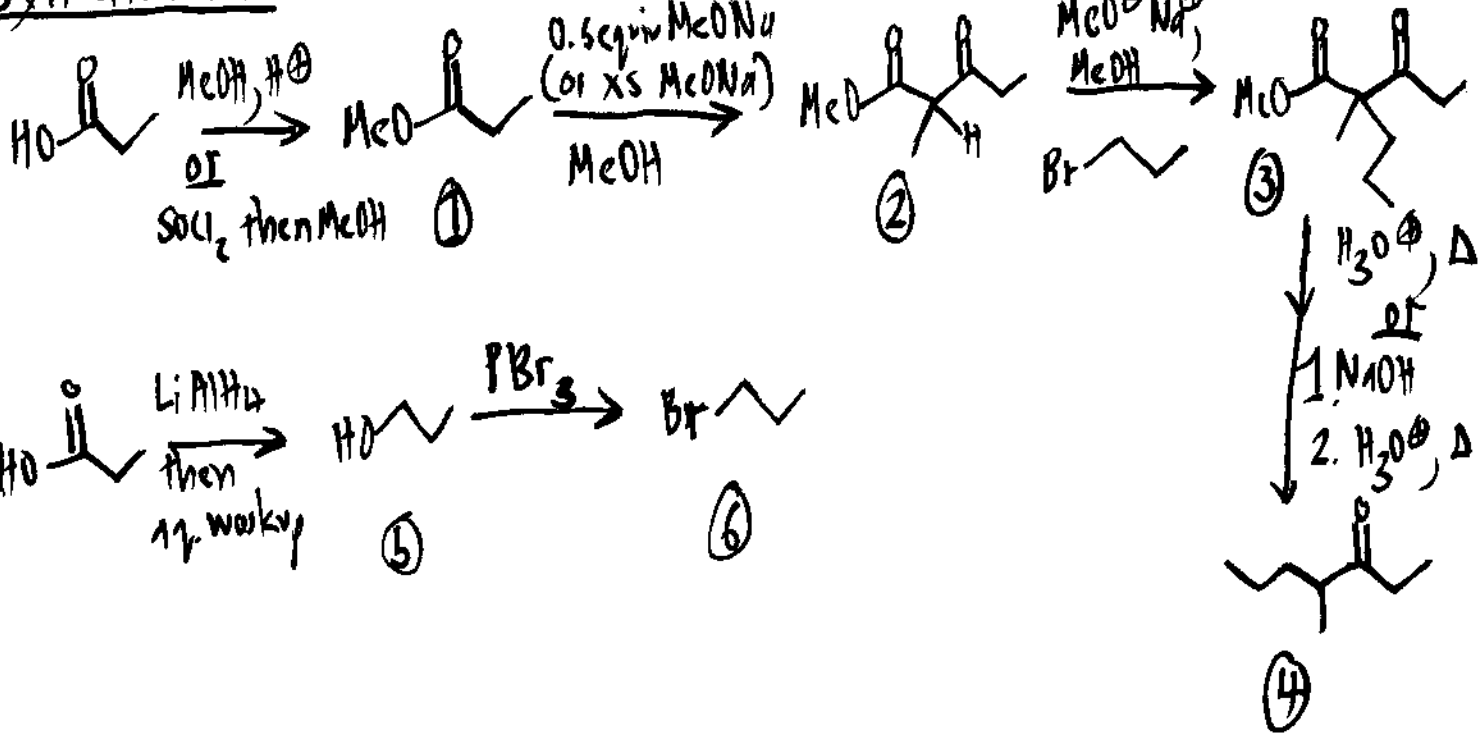
8. Provide the most efficient synthesis (30 points).



from 3 equiv of  and any other reagents

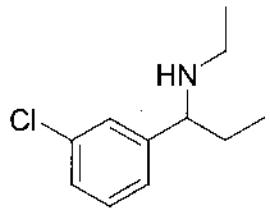


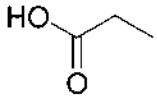
Syn direction!

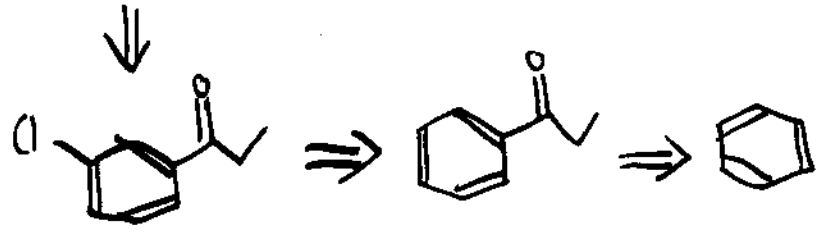


- other routes may be possible

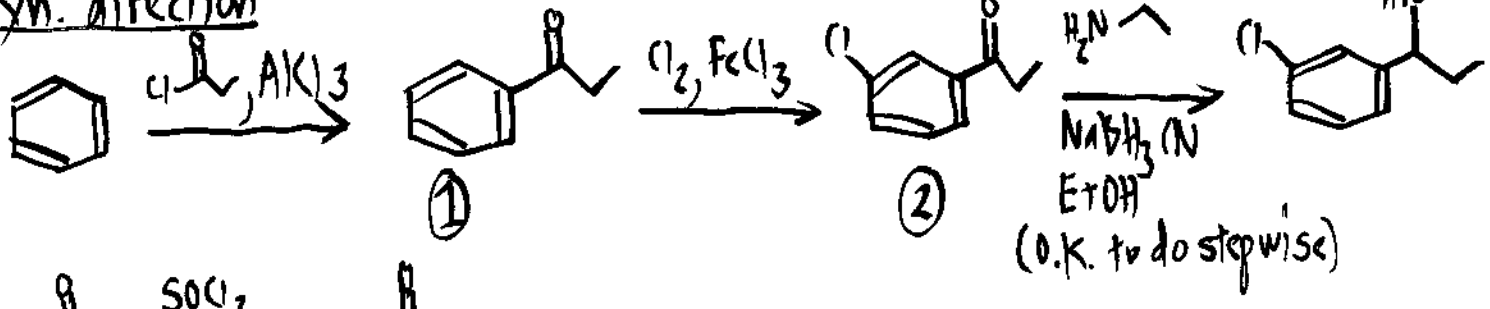
9. Provide the most efficient synthesis (30 points).



from 2 equiv of  and  and any other reagents

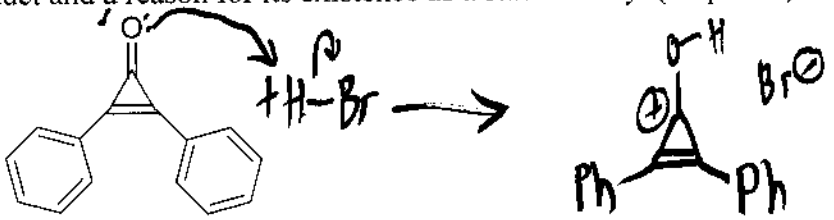


Syn. direction



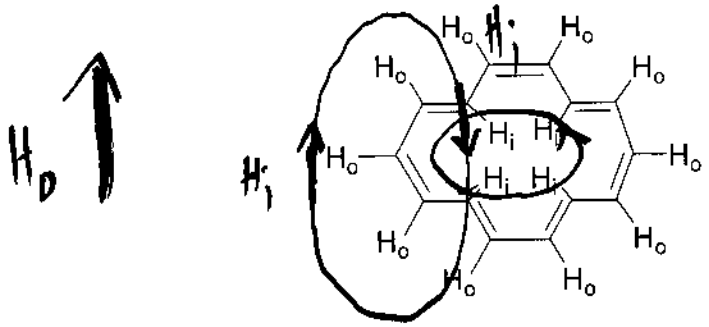
• other routes may be possible

10. The cyclopropenone shown below forms an addition product with HBr that exhibits the properties of an ionic salt. Suggest a structure for this product and a reason for its existence as a stable entity. (15 points).



The ionic salt forms because the cation is aromatic ($2\,e^{\ominus}$)

11. There are two types of hydrogens, H_i and H_o, present in the [14]annulene shown below. In the proton NMR spectra two peaks are observed, one at –0.61 ppm and one at 7.88 ppm. Assign these peaks toeither H_i or H_o. Provide a brief explanation for your answer (15 points).



$H_o = 7.88$ ppm

$H_i = \ominus 0.61$ ppm

The conjugated π-system results in an electronic current as a result of the applied field. The circulating $e^{\ominus}$ results in an induced field H_i that opposes H_o inside the aromatic ring and is with the H_o outside the aromatic ring

Chemistry 3B, Practice Final

Thursday, December 5, 2002

Student name: Answer Key

Student signature: _____

Write TA's name or Lecture Only: _____

1. Please make sure that the exam has 14 pages including this one.
2. Please write your answers in the spaces provided.
3. Write clearly; illegible or ambiguous answers will be considered incorrect.
4. Only writing implements are allowed **(No Calculators)**.

GOOD LUCK!

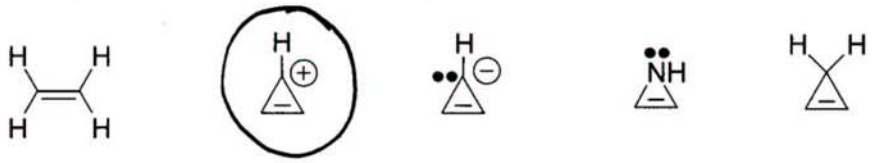
1.	40 points	_____
2.	60 points	_____
3.	60 points	_____
4.	25 points	_____
5.	25 points	_____
6.	30 points	_____
7.	30 points	_____
8.	30 points	_____
9.	30 points	_____
10.	15 points	_____
11.	15 points	_____
Total	**360 points**	_____

MINI-PERIODIC TABLE

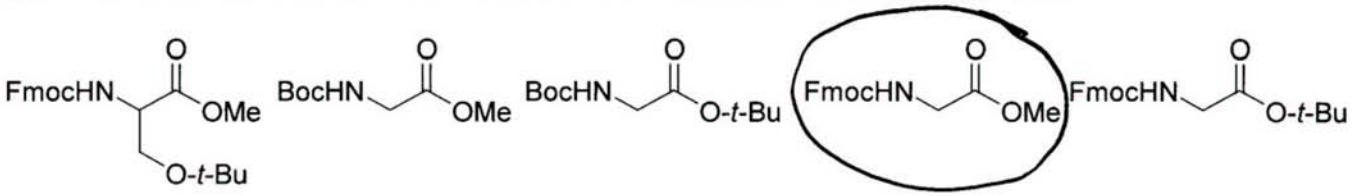
I	II	III	IV	V	VI	VII	VIII
H							He
Li	Be	B	C	N	O	F	Ne
Na	Mg	Al	Si	P	S	Cl	Ar
K	Ca	Ga	Ge	As	Se	Br	Kr

1. Answer the following questions. Every wrong answer cancels a correct answer (40 points total).

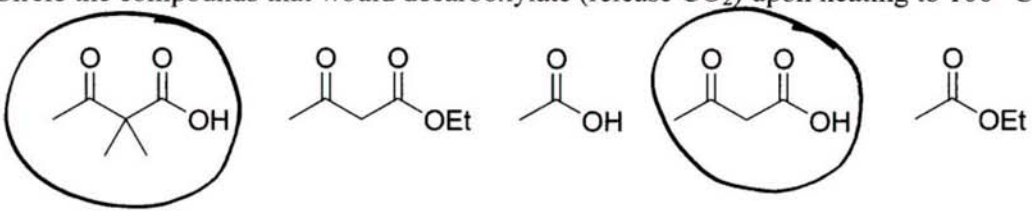
(a). Circle the compounds that are aromatic (7 points).



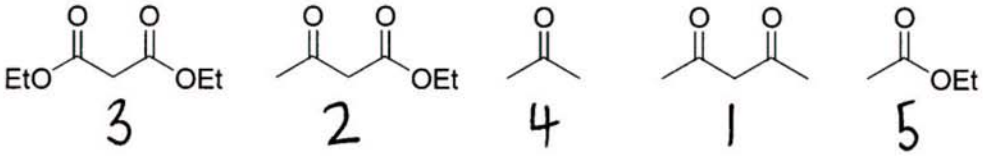
(b). Circle the amino acid derivatives that are stable to trifluoroacetic acid (7 points).



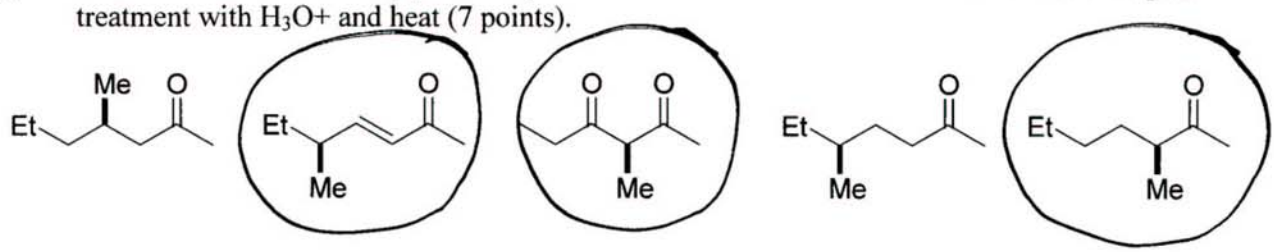
(c). Circle the compounds that would decarboxylate (release CO_2) upon heating to 100 °C (7 points).



(d). Rank the structures from most acidic to least acidic [1 = **most** acidic, 5 = **least** acidic] (7 points).

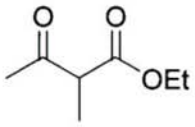


(e). Cricle the enantiomerically pure compounds shown below that would become racemic upon treatment with H_3O+ and heat (7 points).

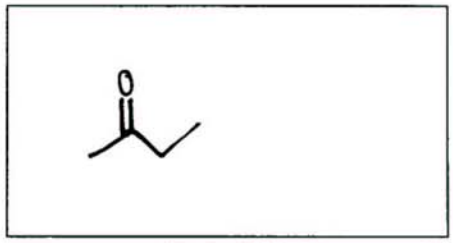


2. For each of the following reactions supply the missing reagents or major organic product in the space provided. If no reaction is expected indicate by N.R. (60 points total, 4 points each question).

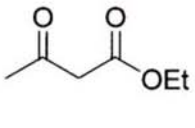
(a)



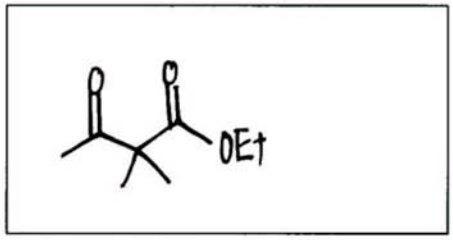
H_3O+, H_2O, Δ



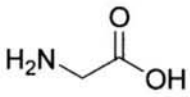
(b)



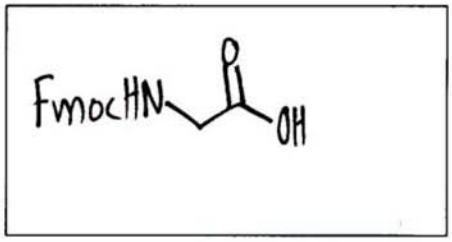
NaOEt (2 equiv),
MeI (2 equiv),
EtOH



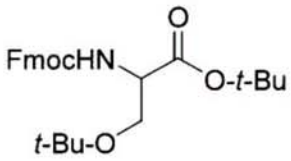
(c)



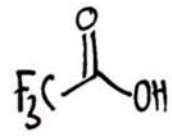
NaOH (1 equiv)
H_2O,
FmocCl

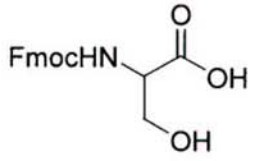


(d)

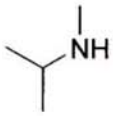


1.

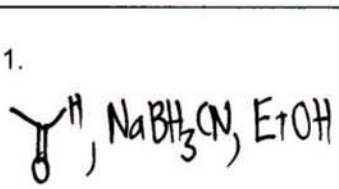


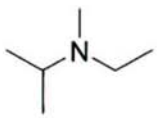


(e)

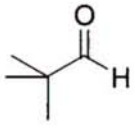


1.

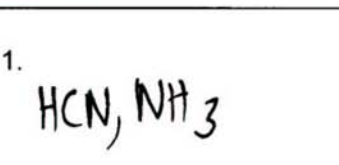


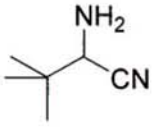


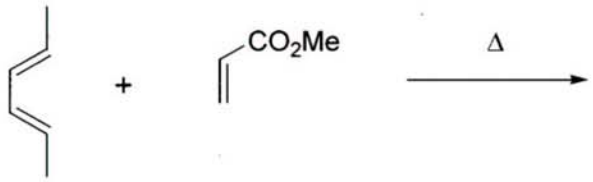
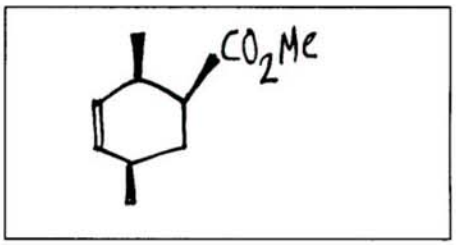
(f)

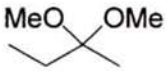
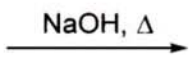
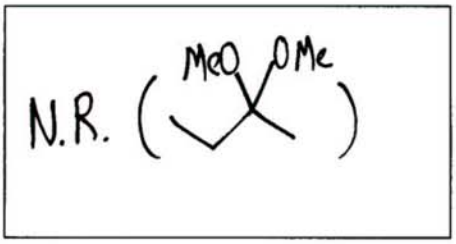


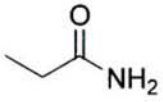
1.

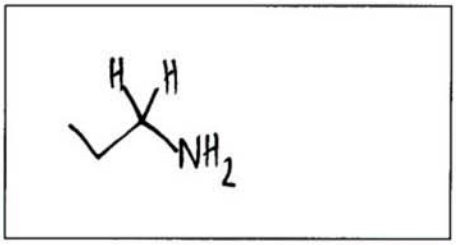


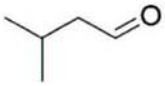


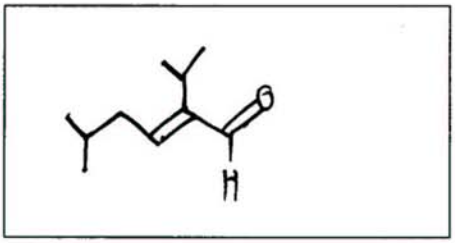
(g) 
CO2Me
Δ

CO2Me

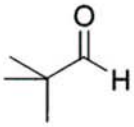
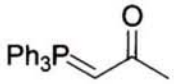
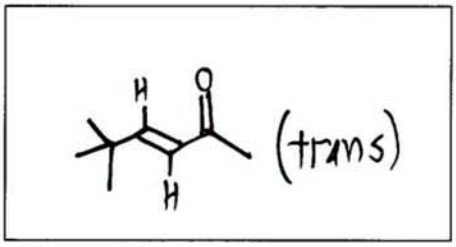
(h) 
MeO
OMe

NaOH, Δ

N.R.
MeO
OMe

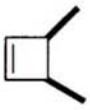
(i) 
O
NH2

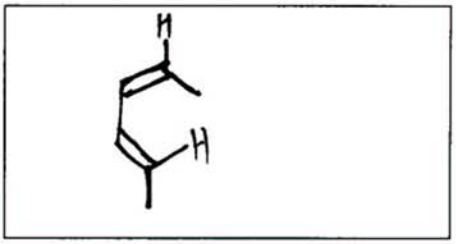
LiAlH4, then
aqueous work-up

H
H
NH2

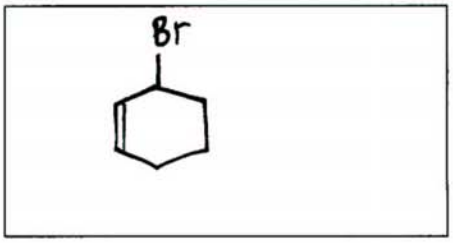
(j) 
O

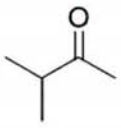
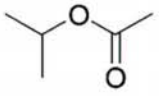
NaOH, H2O, Δ

O
H

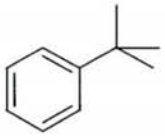
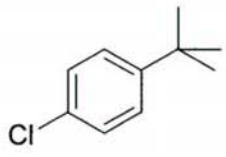
(k) 
O
H

Ph3P
O

H
O
H
(trans)

(l) 

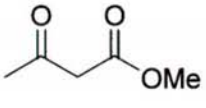
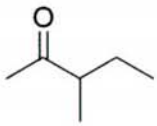
Δ

H
H

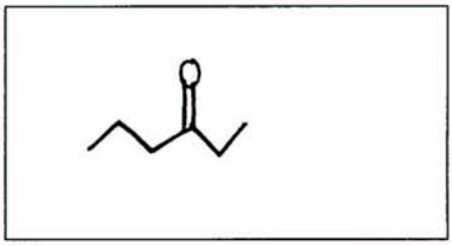
(m)  $\xrightarrow{NBS,\ hv,\ CCl_4}$ 

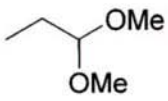
(n)  $\xrightarrow{1.\ F_3C(C=O)OC(=O)H}$ 

(o)  $\xrightarrow{1.\ FeCl_3,\ Cl_2}$ 

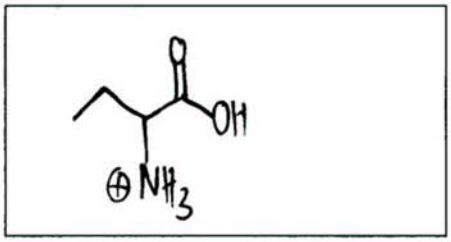
3. For each of the following reactions supply the missing reagents or major organic product in the space provided. If no reaction is expected indicate by N.R. (60 points total, 6 points each question).

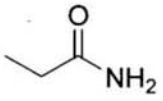
(a)  $\xrightarrow{\begin{array}{l}1.\ NaOMe\ (1\ equiv),\ MeOH,\ CH_3I\\ 2.\ NaOMe\ (1\ equiv),\ MeOH,\ EtI\\ 3.\ H_3O^{\oplus},\ H_2O,\ \Delta\end{array}}$ 

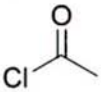
(b)  $\xrightarrow{\begin{array}{l}1.\ LDA\\ 2.\ MeI\\ 3.\ LDA\\ 4.\ EtI\end{array}}$ 

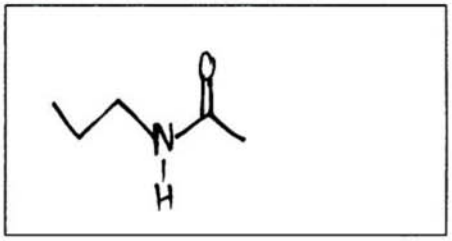
(c) 

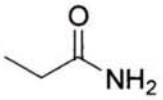
1. H_3O+, H_2O, Δ
2. HCN, NH_3
3. H_3O+, H_2O, Δ

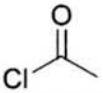


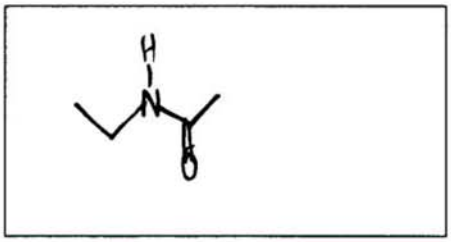
(d) 

1. $LiAlH_4$, then aqueous work-up
2.  , Et_3N



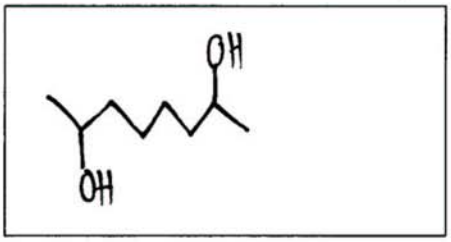
(e) 

1. NaOH, H_2O, Cl_2
2.  , Et_3N



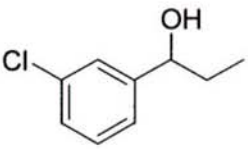
(f) 

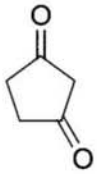
1. O_3, then Zn, AcoH
2. MeLi, then aqueous work-up

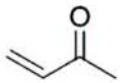


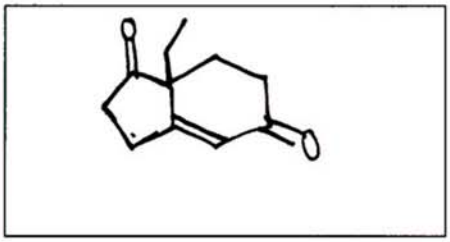
(g) 

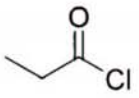
1.  , $AlCl_3$; then aq. work-up
2. $FeCl_3$, Cl_2
3. $NaBH_4$ (or $LiAlH_4$) then aq. work-up



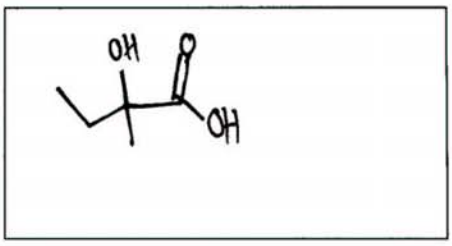
(h) 

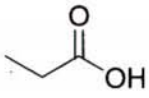
1. NaOMe (1 equiv), MeOH, EtBr
2.  NaOEt, EtOH, Δ



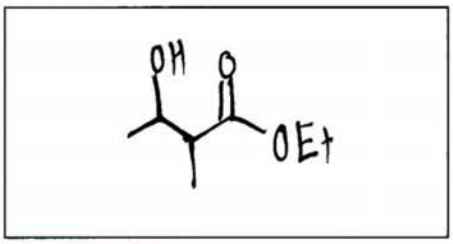
(i) 

1. Me_2CuLi
2. HCN
3. H_3O+, H_2O, Δ

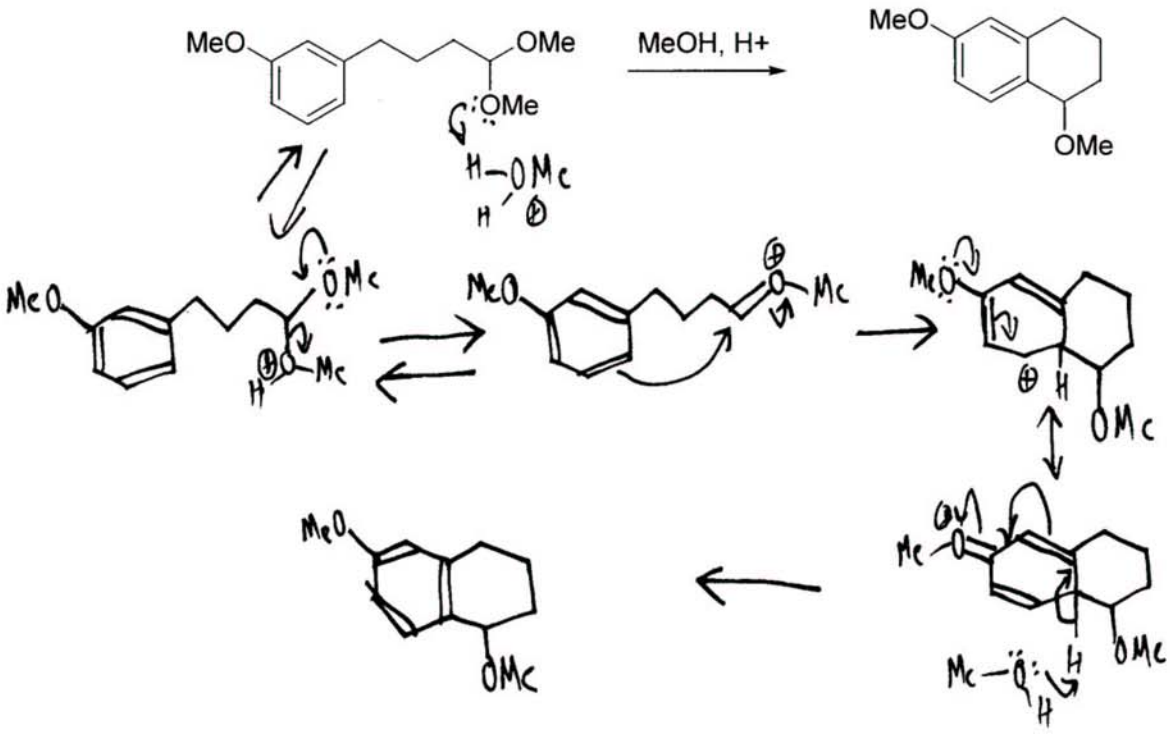


(j) 

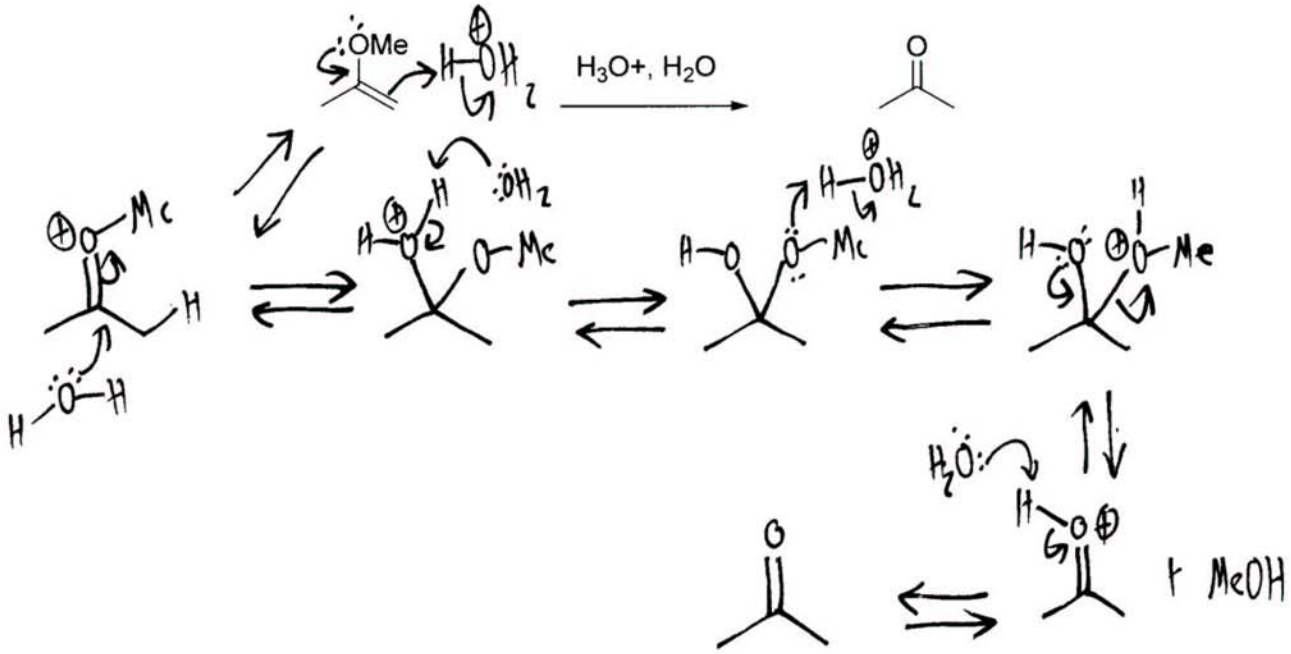
1. EtOH, HCl, Δ
2. LDA
3. CH_3CHO, then aqueous work-up



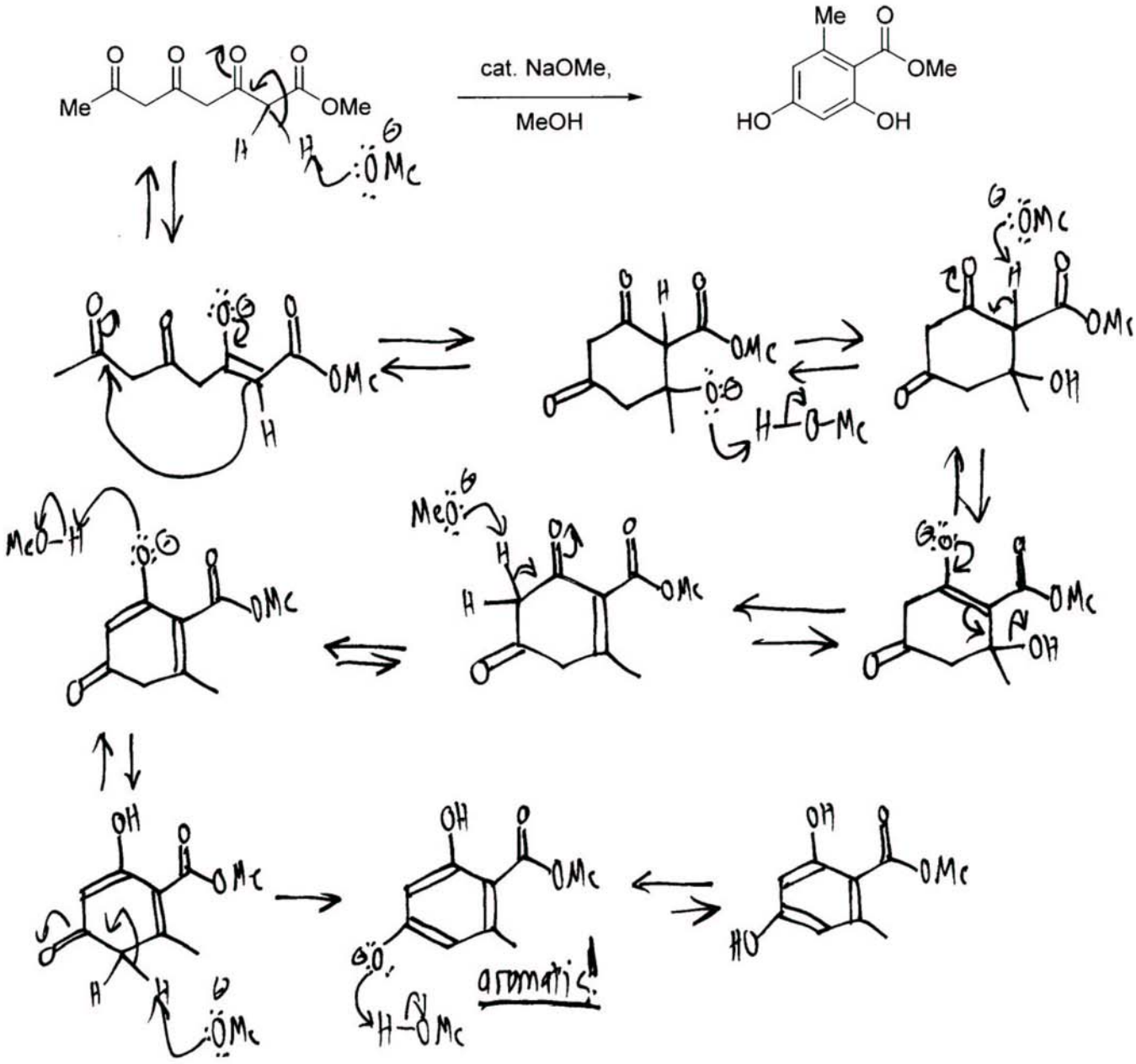
4. Provide a mechanism for the below transformation (25 points).



5. Water and acid readily hydrolyze enol ethers such as the one shown below. Provide a mechanism. (25 points).

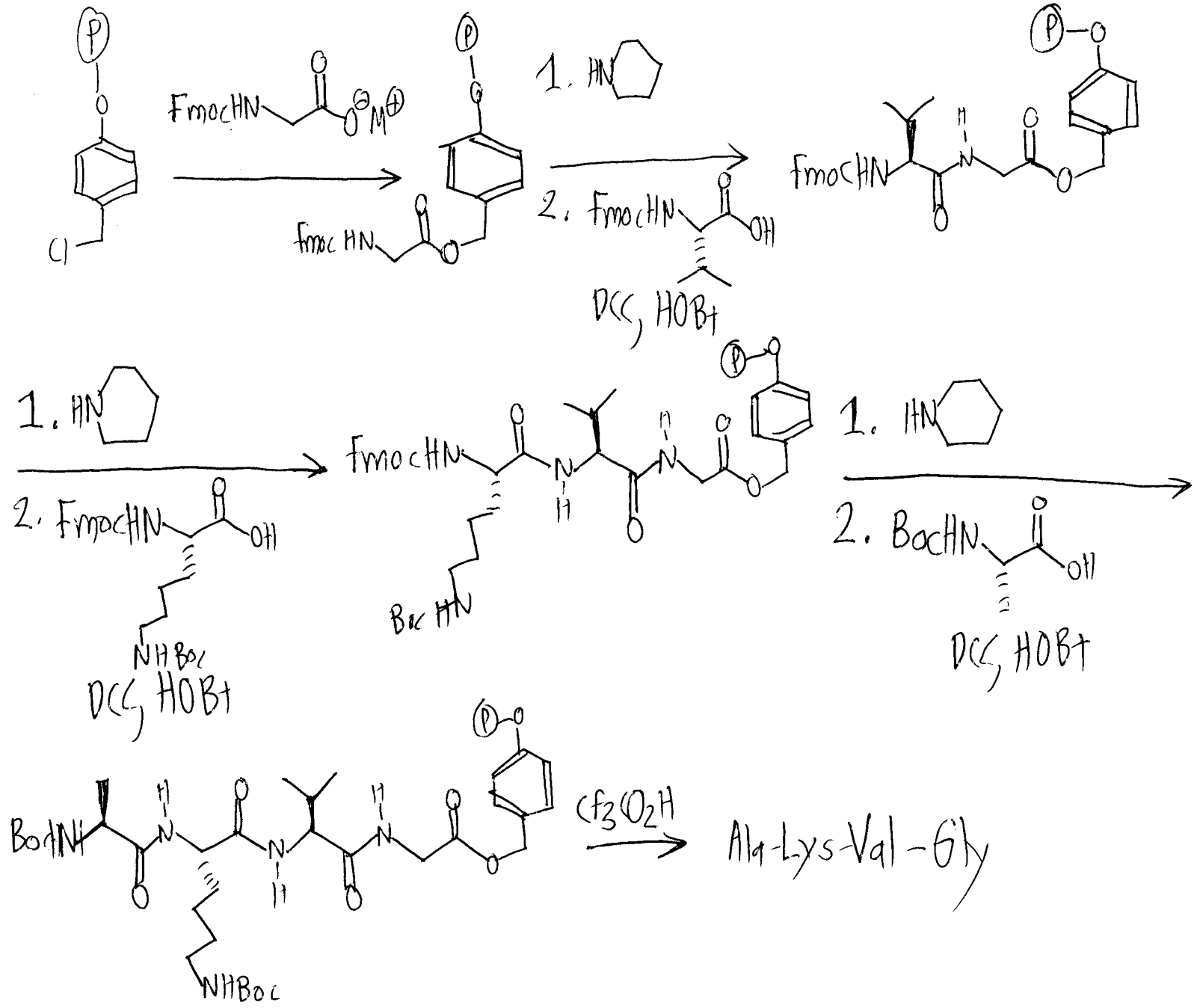


6. Many natural products containing aromatic rings are also biosynthesized by sequential Claisen condensation followed by cyclization to form the aromatic ring. Provide a mechanism for the related transformation provided below (30 points).

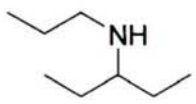


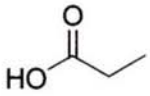
- the order of some steps may be different

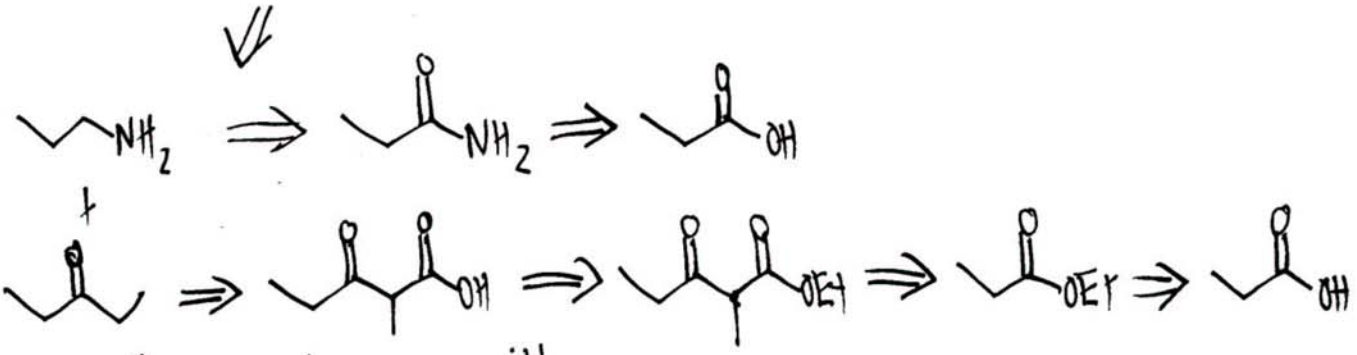
7. Provide a solid-phase synthesis of Ala-Lys-Val-Gly from any protected amino acids (30 points).



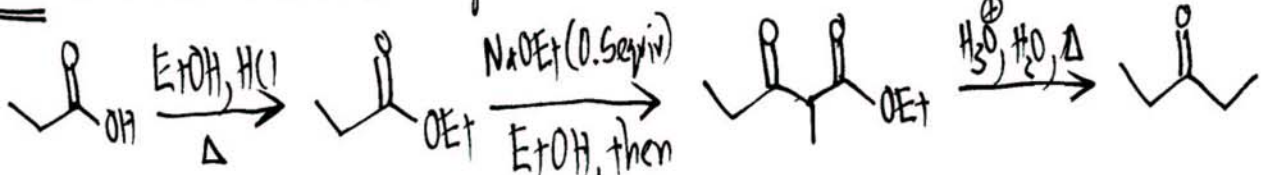
8. Provide the most efficient synthesis (30 points).

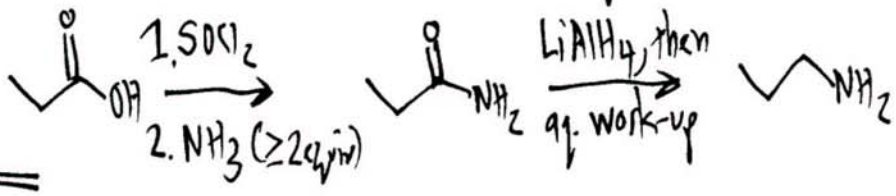


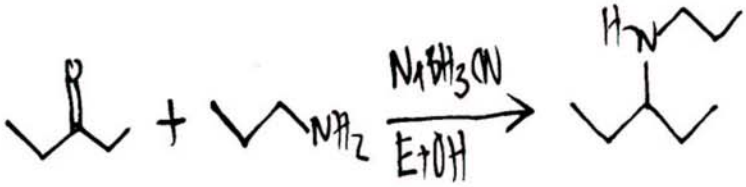
from 3 equiv of  and any other reagents



other disconnections are possible

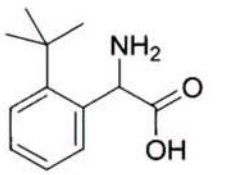




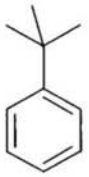


9. Provide the most efficient synthesis of the following amino acid (30 points).

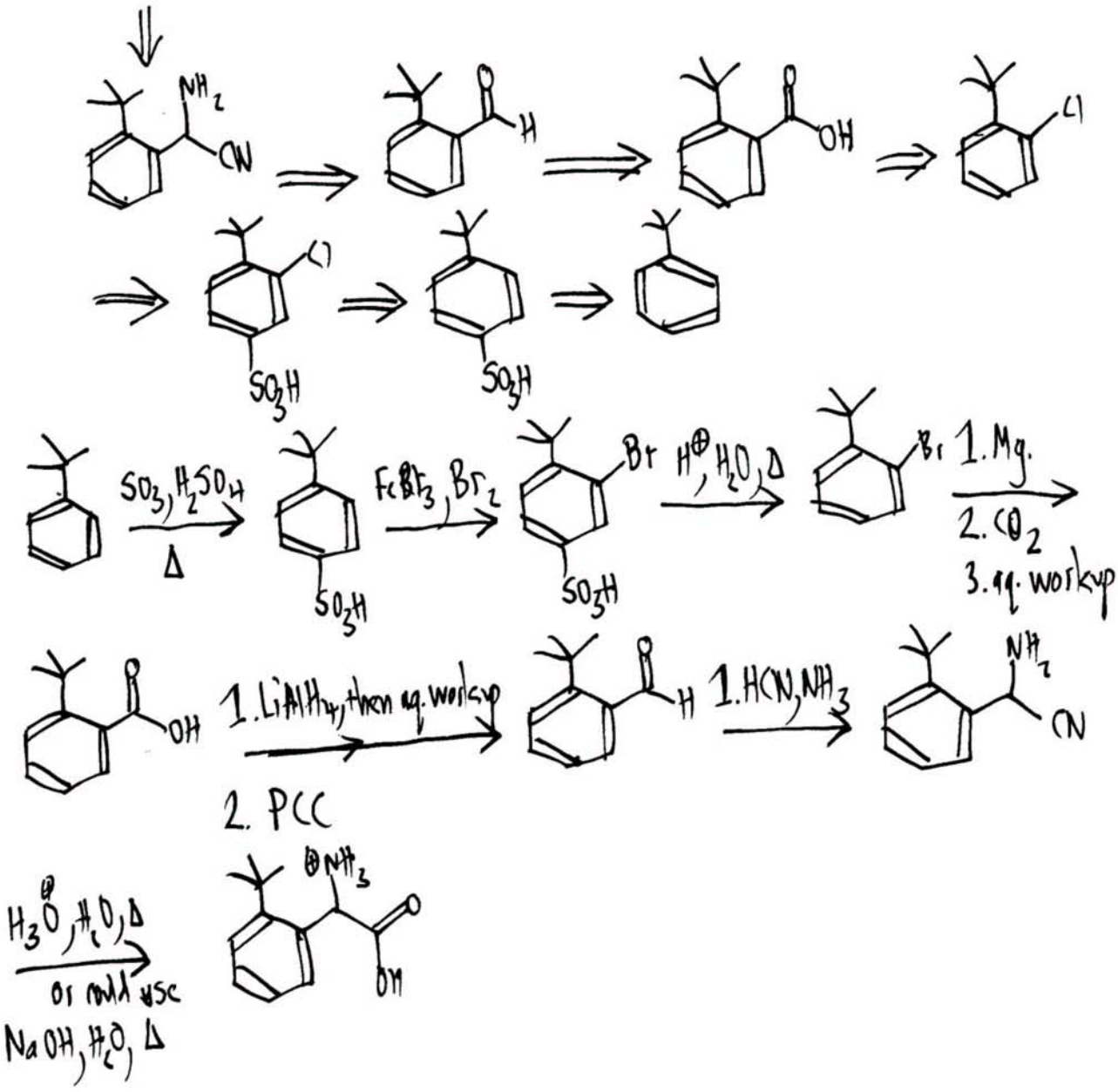
10.



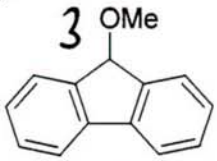
starting from

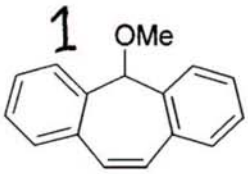


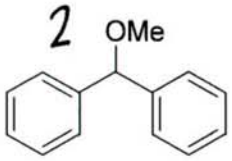
and any other reagents



10. Rank the structures listed below in order of ease of cation formation under acidic conditions [1 = **most** facile ionization, 3 = **least** facile ionization]. Provide a brief explanation for your ranking (15 points).

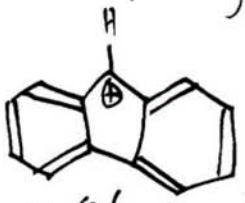




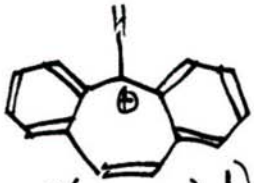


Note that Dr. Sieber used exactly these principles to develop a very popular, highly acid labile linker for solid-phase peptide synthesis.

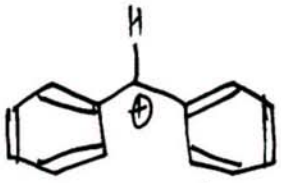
The corresponding cations are drawn below:



$12e^{\ominus}$ (antiaromatic!)



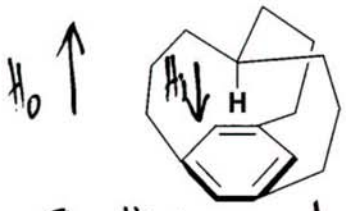
$14e^{\ominus}$ (aromatic!)



nonaromatic

The ease of ionization correlates with the stabilities of the product cations. The aromatic cation is more stable than the nonaromatic cation which is more stable than the antiaromatic cation.

11. The hydrogen highlighted in bold in this strained molecule has a very distinctive chemical shift. Indicate whether it is (a) greater than 10 ppm or (b) less than 0 ppm. Provide a brief explanation of your answer (15 points).



(b) less than 0 ppm. The H_i induced produced by the aromatic ring current opposes the applied field (H_o) and therefore shields the proton.