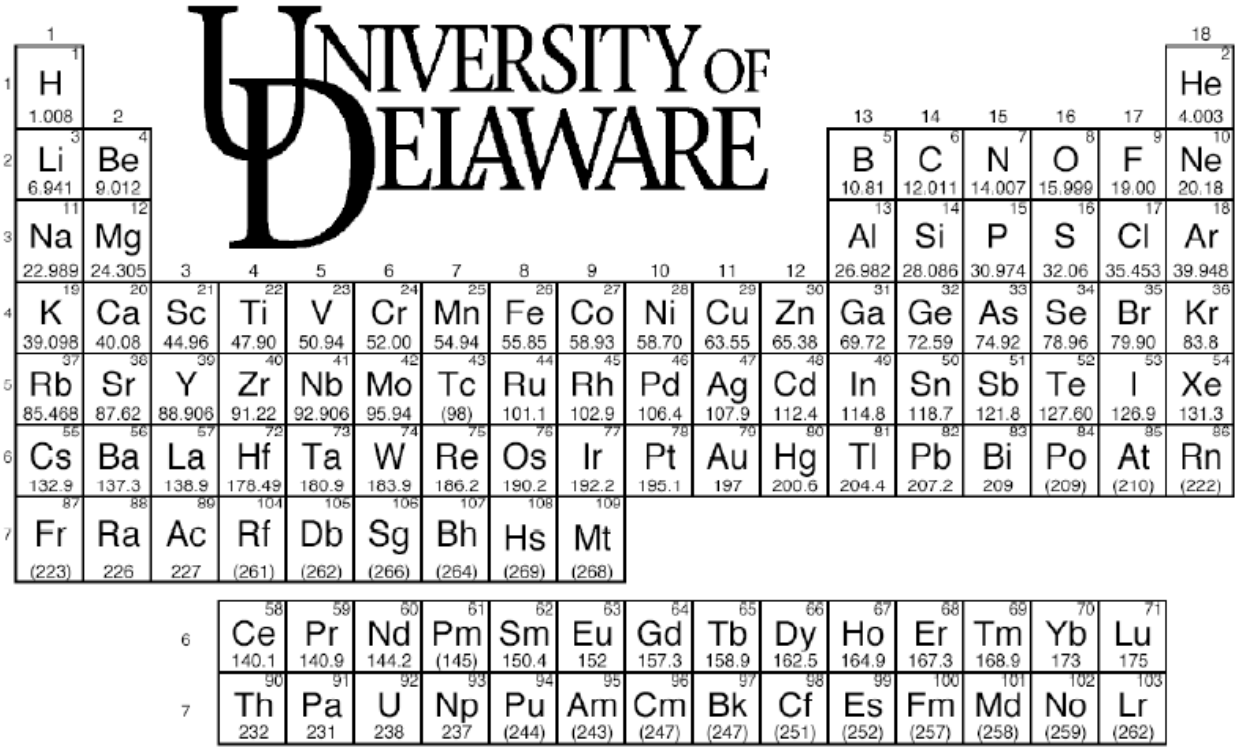
Name:_____

(Print your name clearly!)

Sametz: CHEM 322 Spring 2012

Organic Chemistry Final

All answers should be written CLEARLY in the space provided. (If it's not clear, it's wrong).



	1												13	14	15	16	17	18
1	H 1.008																	He 4.003
2	Li 6.941	Be 9.012											B 10.81	C 12.011	N 14.007	O 15.999	F 19.00	Ne 20.18
3	Na 22.989	Mg 24.305	3	4	5	6	7	8	9	10	11	12	Al 26.982	Si 28.086	P 30.974	S 32.06	Cl 35.453	Ar 39.948
4	K 39.098	Ca 40.08	Sc 44.96	Ti 47.90	V 50.94	Cr 52.00	Mn 54.94	Fe 55.85	Co 58.93	Ni 58.70	Cu 63.55	Zn 65.38	Ga 69.72	Ge 72.59	As 74.92	Se 78.96	Br 79.90	Kr 83.8
5	Rb 85.468	Sr 87.62	Y 88.906	Zr 91.22	Nb 92.906	Mo 95.94	Tc (98)	Ru 101.1	Rh 102.9	Pd 106.4	Ag 107.9	Cd 112.4	In 114.8	Sn 118.7	Sb 121.8	Te 127.60	I 126.9	Xe 131.3
6	Cs 132.9	Ba 137.3	La 138.9	Hf 178.49	Ta 180.9	W 183.9	Re 186.2	Os 190.2	Ir 192.2	Pt 195.1	Au 197	Hg 200.6	Tl 204.4	Pb 207.2	Bi 209	Po (209)	At (210)	Rn (222)
7	Fr (223)	Ra 226	Ac 227	Rf (261)	Db (262)	Sg (266)	Bh (264)	Hs (269)	Mt (268)									

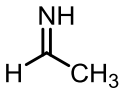
6	Ce 140.1	Pr 140.9	Nd 144.2	Pm (145)	Sm 150.4	Eu 152	Gd 157.3	Tb 158.9	Dy 162.5	Ho 164.9	Er 167.3	Tm 168.9	Yb 173	Lu 175
7	Th 232	Pa 231	U 238	Np 237	Pu (244)	Am (243)	Cm (247)	Bk (247)	Cf (251)	Es (252)	Fm (257)	Md (258)	No (259)	Lr (262)

FOR QUESTIONS 9-10: read the instructions carefully regarding checking the "skip" boxes. You need to do 3 questions per page for Question 9, and 4 questions per page for #10.

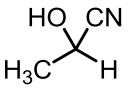
You may raise your hand to ask a question if you are unsure what a question is asking of you.

Part I: Multiple Choice (8 points)

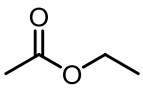
Consider the following compounds and answer questions 1-4.



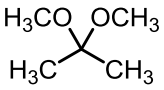
a



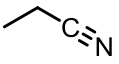
b



c



d

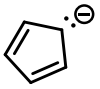


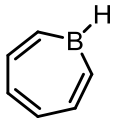
e

1. Which is a **cyanohydrin**?	a	b	c	d	e
2. Which is an **imine**?	a	b	c	c	d
3. Which would be converted to a **ketone** upon acid hydrolysis?	a	b	c	d	e
4. Which could be **saponified**?	a	b	b	d	e

Part II: Short Answer

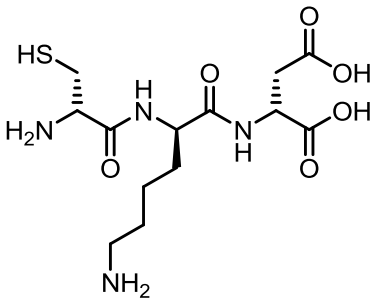
5. (5 points) For each of the species below, indicate whether it is aromatic, antiaromatic, or neither.





6. (5 points) The tripeptide Cys-Lys-Asp (Cysteine-Alanine-Aspartic acid) is shown below. However, depending on pH the acidic and/or basic functional groups on the molecule may be either protonated or deprotonated. Redraw the **entire** molecule to reflect the major species expected at physiological pH (approximately 7.4), with functional groups suitably protonated and/or deprotonated.

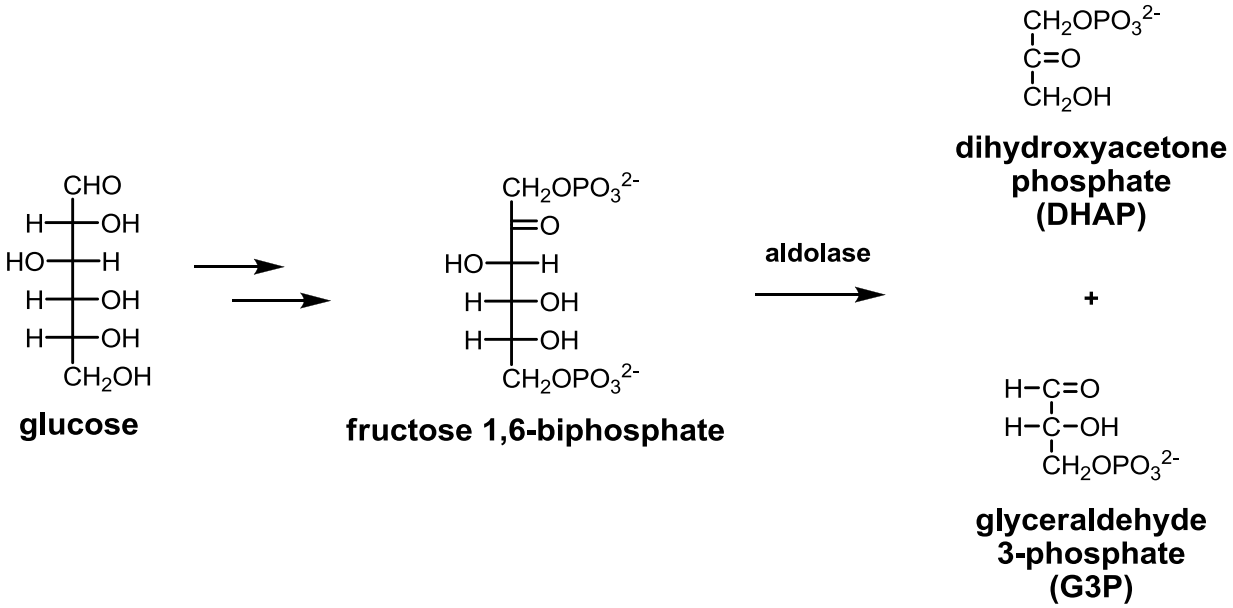
Hint: no calculations required. A rough idea of the pKas of the functional groups involved should suffice.



7. (10 points) Choose **one** of the five reactions below. Show the product of the reaction described, and give a reasonable reaction mechanism to account for its formation. Note: this question is also testing you on nomenclature. Partial credit may be given for a reasonable mechanism and product if your reactants/reagents aren't quite correct.

- Mutarotation of α-glucopyranose to β-glucopyranose
- Saponification of 2-oxacyclohexanone
- Claisen condensation of ethyl ethanoate, using sodium ethoxide as base catalyst
- Sulfonation of anisole {mechanism must explain the regioselectivity of the reaction, i.e. o,p- or m- major product(s) }
- Acid-catalyzed epimerization (racemization) of (*R*)-3-methyl-2-pentanone
- Acid-catalyzed reaction of propanal with methanol to form an acetal

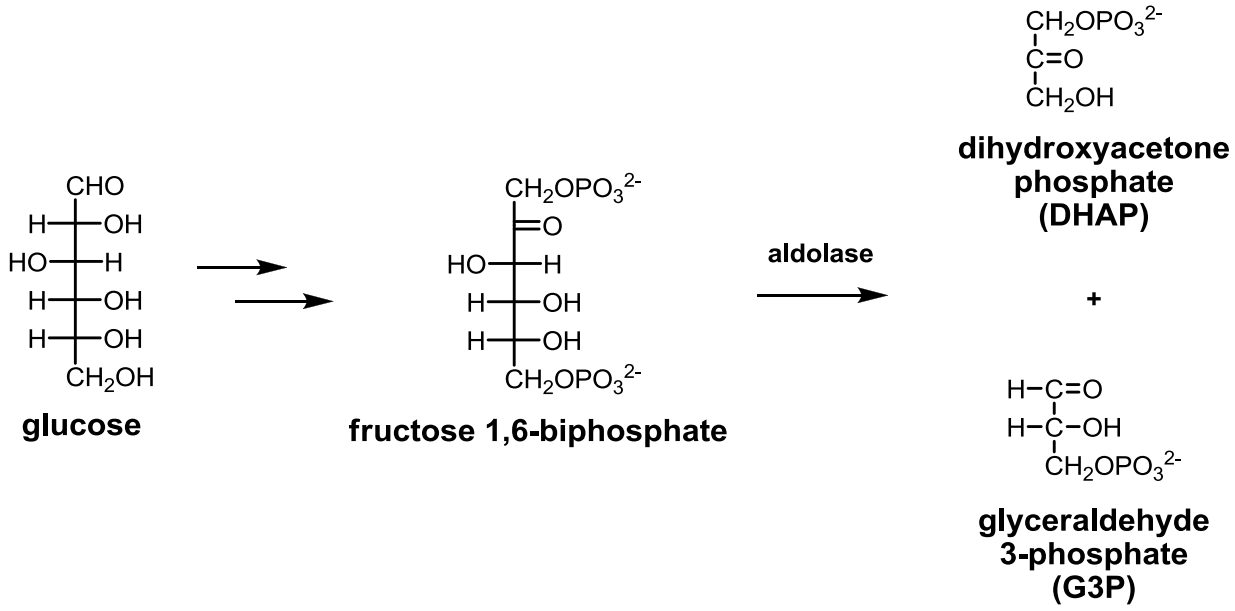
8. (17 points total) Shown below are transformations involved in the biochemical pathway known as glycolysis:



a) (9 points) Although glucose and fructose 1,6-biphosphate are shown as acyclic Fisher projections, in solution they favor cyclic hemiacetals. Draw Haworth projections for:

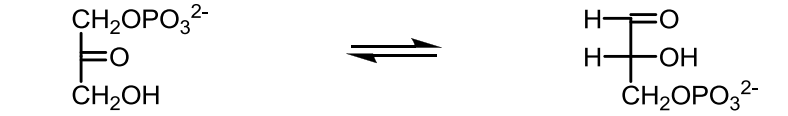
i) α-glucopyranose

ii) fructose 1,6-biphosphate in the β-furanose form.



b) (4 points) Give a reasonable mechanism for the conversion of fructose 1,6-biphosphate to DHAP and G3P. Hint: you can choose to use either acid or base catalysis for your mechanism.

(The actual mechanism is more intricate as well as enzyme-specific, but in principle it can occur without the enzyme just using the chemistry you learned in CHEM322).



dihydroxyacetone phosphate (DHAP)

glyceraldehyde 3-phosphate (G3P)

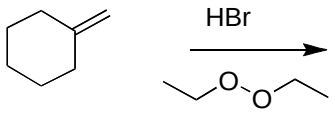
c) (4 points) Give a reasonable mechanism for the conversion of DHAP to G3P. Again, a "simple" CHEM322 mechanism will suffice.

Part IV: Reactions

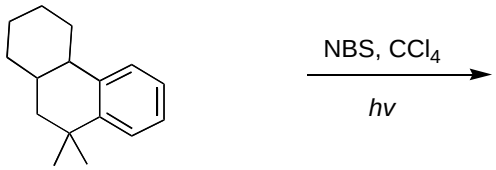
9. (48 points) Give the major organic product(s) for the following reactions. **On each page (Parts A through D), you may check TWO questions to skip and DO THE REMAINING THREE.**

Part A

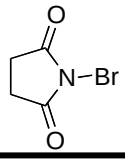
a) ❑SKIP this one



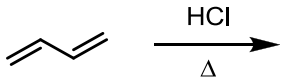
b) ❑SKIP this one



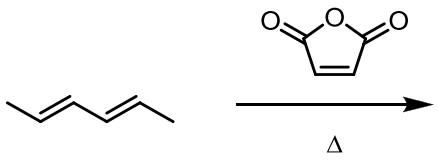
Hint: NBS =



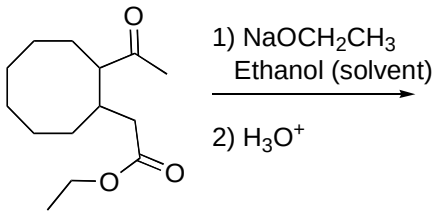
c) ❑SKIP this one



d) ❑SKIP this one

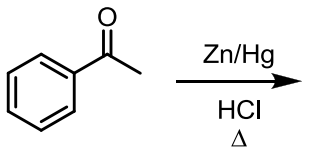


e) ❑SKIP this one



Part B

f) ❑SKIP this one



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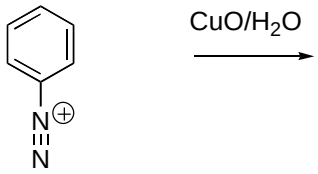

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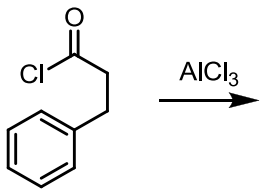
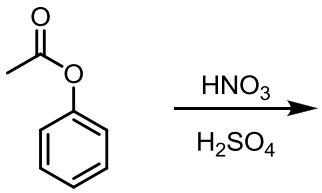


i) ❑SKIP this one



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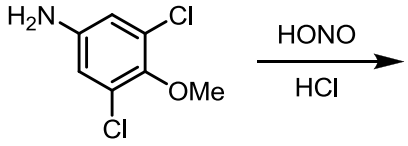
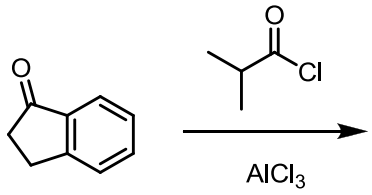
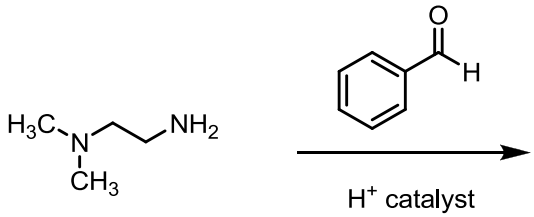


Part C

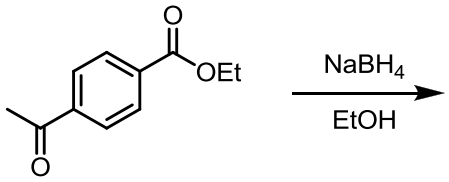
k) ❑SKIP this one



l) ❑SKIP this one



m) ❑SKIP this one



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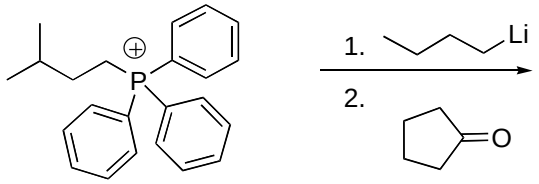
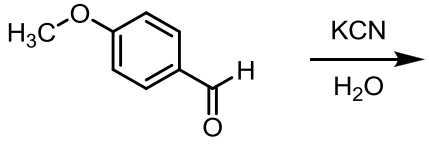
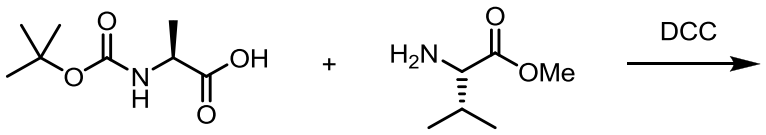


o) ❑SKIP this one

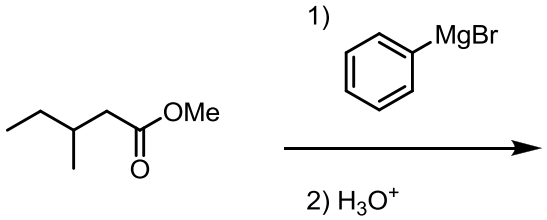


Part D

p) ❑SKIP this one



q) ❑SKIP this one



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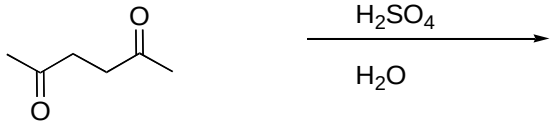

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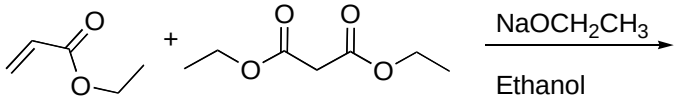

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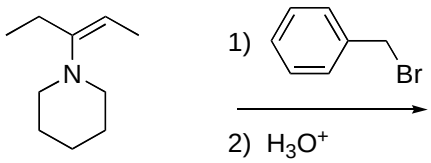
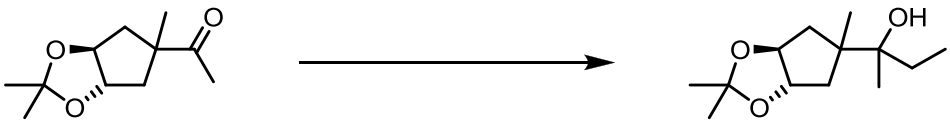


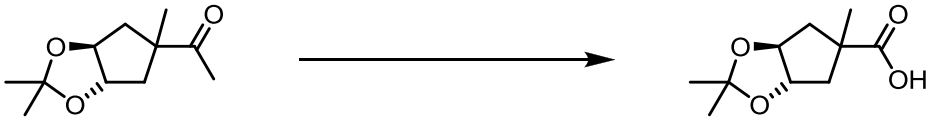
10. (24 points) Provide reagents that would effect the following transformations. **On each page (Parts A and B), you may check ONE question to skip and DO THE REMAINING FOUR.**

Part A

a) ❑SKIP this one



b) ❑SKIP this one



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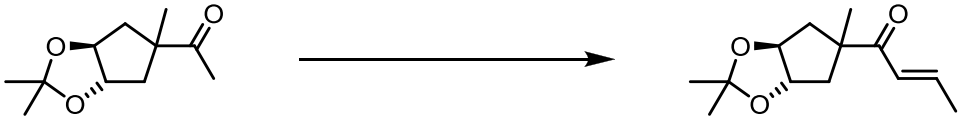
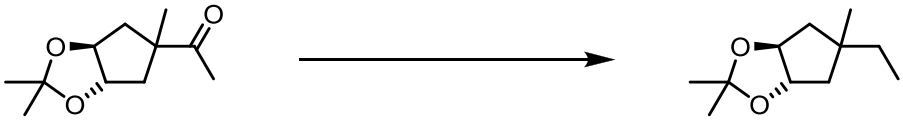
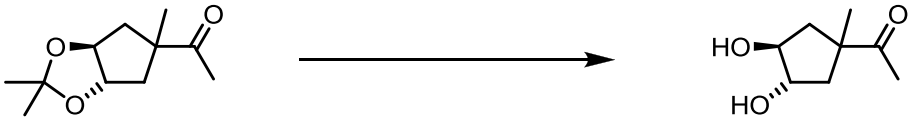


d) ❑SKIP this one

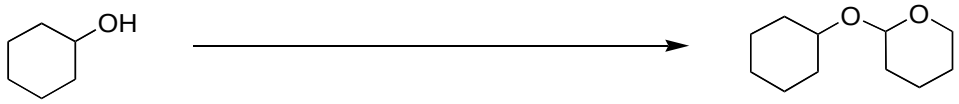


e) ❑SKIP this one

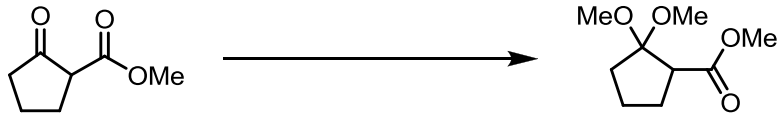


Part D

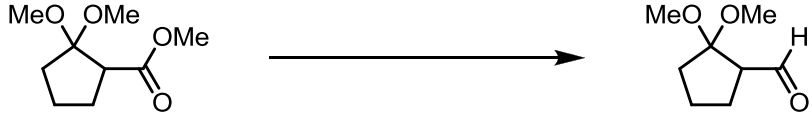
f) ❑SKIP this one



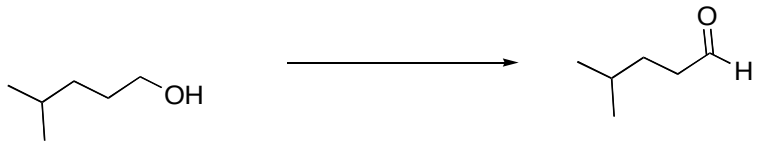
g) ❑SKIP this one



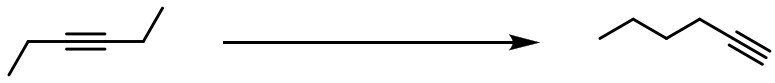
h) ❑SKIP this one



i) ❑SKIP this one



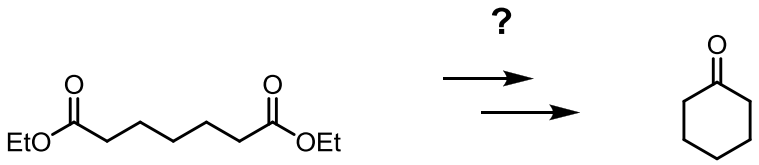
j) ❑SKIP this one



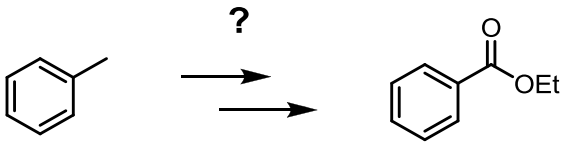
Part V Multistep Synthesis (16 points)

11. (6 points) Multistep synthesis Propose an efficient synthesis for **ONE** of the two compounds below on the right from the starting material on its left. Please draw the structures of the intermediate reaction products. (Just the product, not the mechanism) **CLEARLY** indicate which of the two you wish to be graded; if it's not clear to the grader, they will choose one to grade.

a)

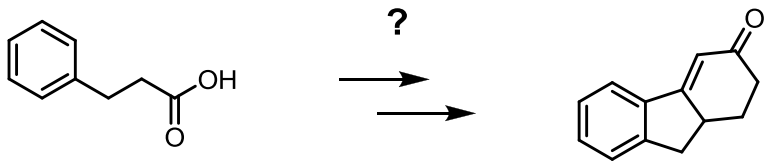


b)

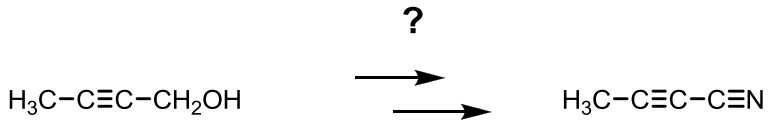


12. (12 points) Choose **ONE** of the following two synthesis problems, and provide a sequence of reactions that will synthesize the compound on the right from the starting material on the left. Draw out the structures of the intermediate reaction products. If you show work on both, **CLEARLY** indicate which of the two you wish to be graded; if it's not clear to the grader, they will choose one to grade.

a)



b)

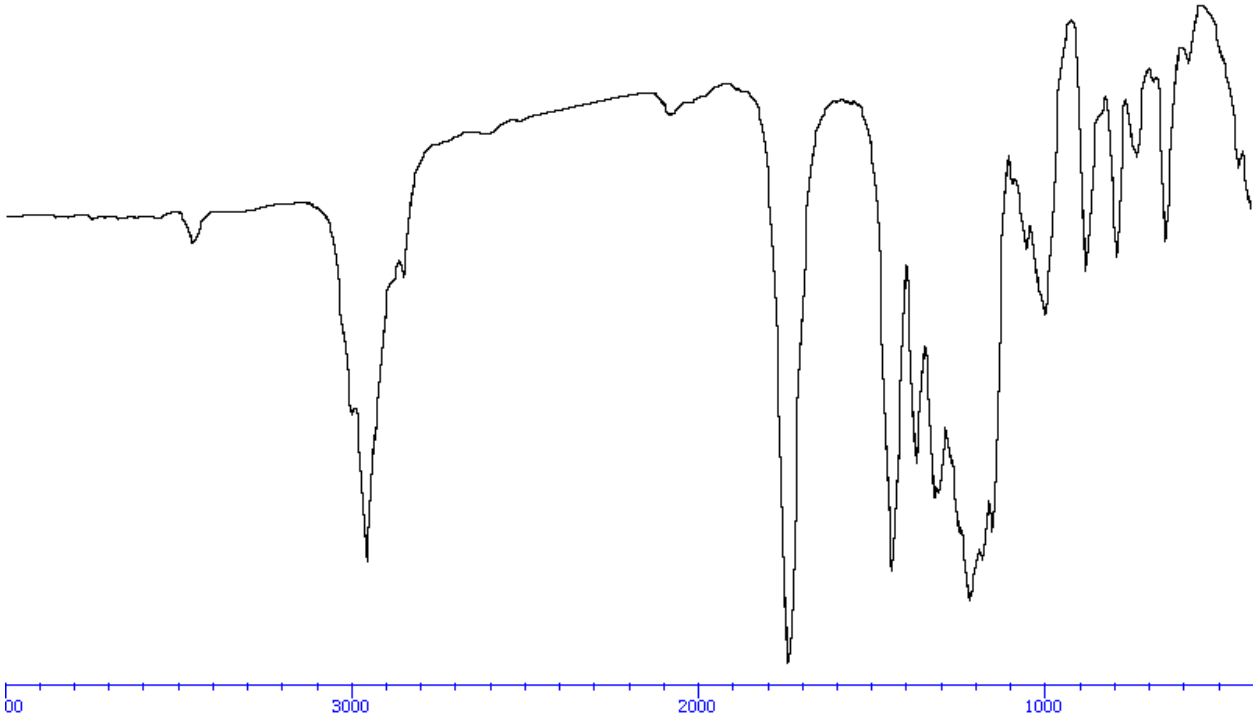


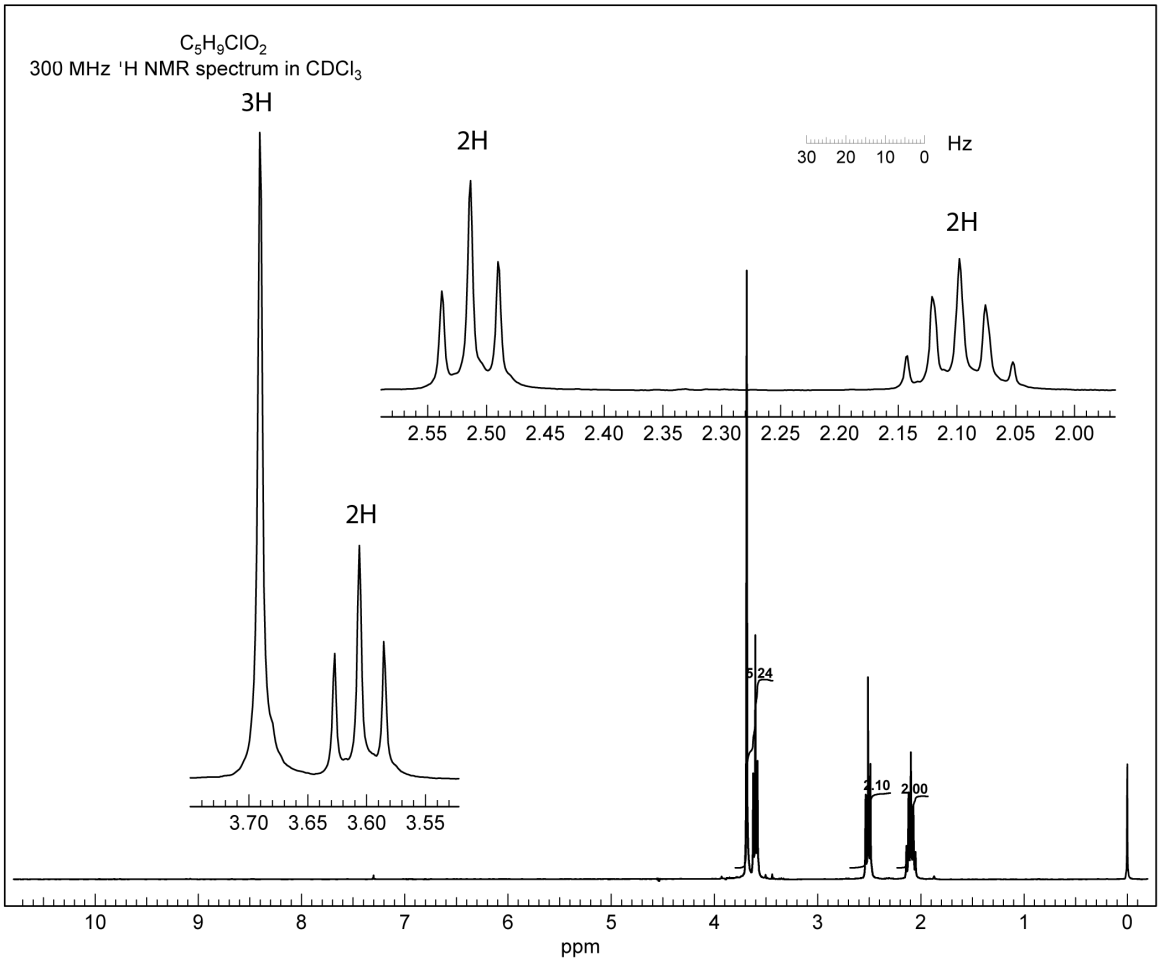
Caution: Both syntheses require approximately the same number of steps, and are of comparable difficulty.

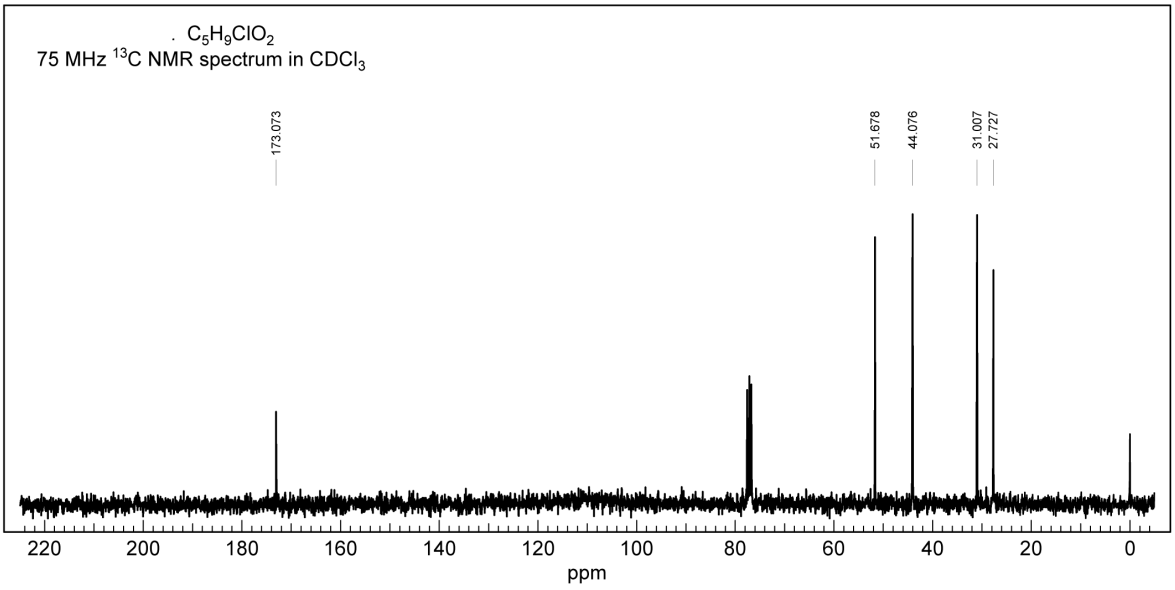
Part VI: Spectroscopic Analysis of an Unknown Compound (15 points)

13. The ^{1}H and ^{13}C NMR spectra for a compound with the formula $C_5H_9ClO_2$ are shown on the next page. The integrations for the signals ("3H", etc.) are shown next to their expansions above the spectrum. In the ^{13}C NMR spectrum on the next page, the signals that correlate with carbons in the unknown are marked with their chemical shift. The IR spectrum for the compound is shown below. Identify the structure of the compound.

Use the ^{1}H NMR data to construct a table (chemical shift, integration, multiplicity, assignment) to identify structural fragments, then arrive at the structure. **You are being graded on your analysis**. Any use of the degrees of unsaturation (also called DBE or IHD), IR, or ^{13}C NMR will be considered for extra credit.



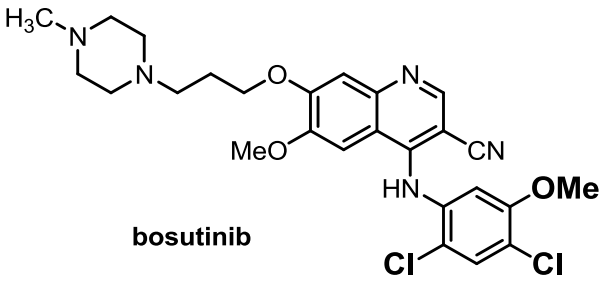

C5H9ClO2
300 MHz 'H NMR spectrum in CDCl3
3H
2H
2H
2H
Hz
30 20 10 0
2.55 2.50 2.45 2.40 2.35 2.30 2.25 2.20 2.15 2.10 2.05 2.00
3.70 3.65 3.60 3.55
5.24
2.10
2.00
10 9 8 7 6 5 4 3 2 1 0
ppm


. C5H9ClO2
75 MHz 13C NMR spectrum in CDCl3
173.073
51.678
44.076
31.007
27.727
220 200 180 160 140 120 100 80 60 40 20 0
ppm

(extra page for Problem 14 work)

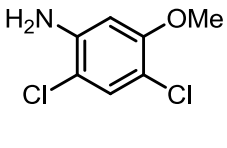
Extra credit (20 points)

16. Bosutinib is a drug currently in Phase III clinical trials to treat leukemia. It is an inhibitor of certain enzymes called kinases, and is also used as a biochemical tool. Recently it has been discovered that some of the material being sold as bosutinib are actually structural isomers that differ in the placement of the chlorine and methoxy groups (indicated by bold characters) on the aniline ring.

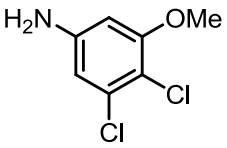


bosutinib

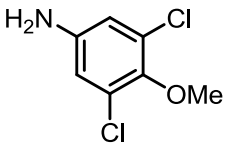
One of the reactants used in the synthesis of the molecule is 2,4-dichloro-5-methoxy aniline (structure **B** below). **B** is sold by several vendors, and current suspicion is that some of these outfits were actually synthesizing and manufacturing isomers of **B** mistakenly. Two of the suspected isomers, **X** and **Y**, are shown below. It is odd that such a mistake could have spread on a global scale, particularly because even a CHEM322 student should be able to distinguish between the three by ^{1}H NMR.



B



X



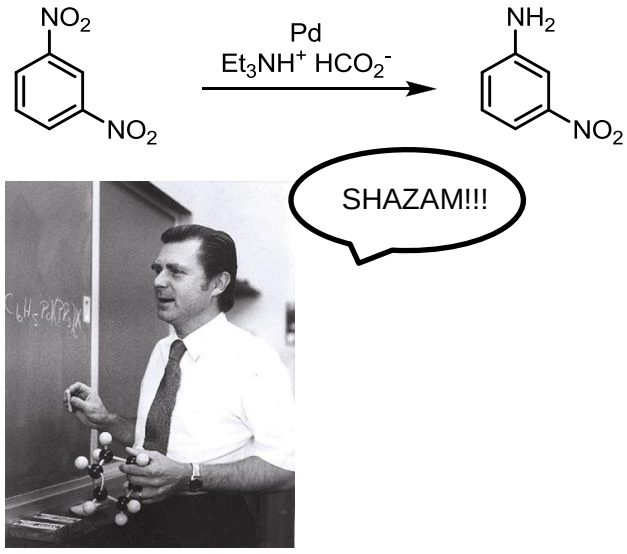
Y

a) (4points) The ^{1}H NMR spectrum of **Y** should be clearly distinct from **B** (as well as **X**). Explain how you would be able to distinguish **Y** from the others.

b) (2 points) A spectrometer with decent resolution should allow you to distinguish between **B** and **X** as well. What feature would you expect to see in the spectrum of **X** and not **B**?

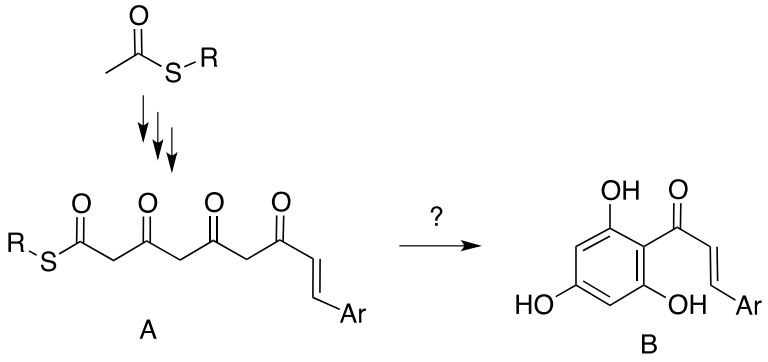
c) (8 points) Propose a synthesis of **B** from benzene.

Okay, this one's a little tough. Fortunately you have a Blue Hen Nobel Laureate in chemistry to help you with this problem. Prof. Richard Heck reported in 1980 that one of the two nitro groups of *m*-dinitrobenzene could be reduced to give *m*-nitroaniline:

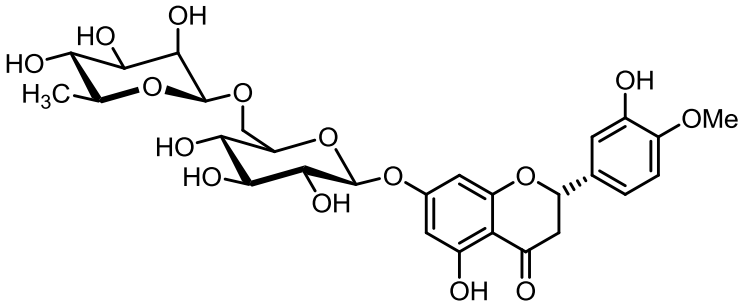


Your task now simplifies to: synthesize dinitrobenzene from benzene, and then convert *m*-nitroaniline to **B**.

17. a) (4 points) Chalcones are an important class of natural products derived from polyketides. Chalcone B is derived from polyketide A via a Claisen reaction. Draw the mechanism for the conversion of A to B. (Hint: remember that phenols can be thought of as very stable enols. Consider drawing B in its fully keto form.).

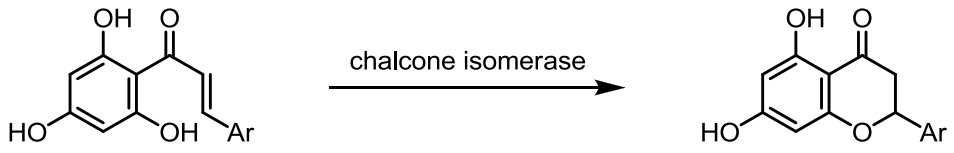


17b) (2 points) Hesperidin is a compound found in citrus fruits. It is an example of a class of compounds called *flavonoids*.



hesperidin

The core structure, a **flavanone**, is biosynthesized from the corresponding chalcone by a *chalcone isomerase* enzyme:



a chalcone **a flavanone**

This reaction is essentially the same as one that you learned in CHEM 322—one that has a person's name attached to it. Give the name of the reaction as well as a mechanism.

Approximate ^{1}H NMR Chemical Shifts

Hydrogen	δ (ppm)
CH_3	0.8–1.0
CH_2	1.2–1.5
CH	1.4–1.7
$C{=}C{-}CH_x$	1.7–2.3
$O{=}C{-}CH_x$	2.0–2.7
$Ph{-}CH_x$	2.3–3.0
$\equiv C{-}H$	2.5
$R_2N{-}CH_x$	2.0–2.7
$I{-}CH_x$	3.2
$Br{-}CH_x$	3.4
$Cl{-}CH_x$	3.5
$F{-}CH_x$	4.4
$O{-}CH_x$	3.2–3.8
C=CH	4.5–7.5
Ar–H	6.8–8.5
O=CH	9.0–10.0
ROH	1.0–5.5
ArOH	4.0–12.0
RNH_x	0.5–5.0
$CONH_x$	5.0–10.0
RCOOH	10–13

Approximate ^{13}C NMR Chemical Shifts

Carbon	δ (ppm)
Alkanes	
Methyl	0–30
Methylene	15–55
Methine	25–55
Quaternary	30–40
Alkenes	
C=C	80–145
Alkynes	
C≡C	70–90
Aromatics	110–170
Benzene	128.7
Alcohols, Ethers	
C–O	50–90
Amines	
C–N	40–60
Halogens	
C–F	70–80
C–Cl	25–50
C–Br	10–40
C–I	–20–10
Carbonyls, C=O	
$R_2C{=}O$	190–220
RXC=O (X = O or N)	150–180

Approximate IR Absorption Frequencies

Bond	Frequency (cm^{-1})	Intensity
O–H (alcohol)	3650–3200	Strong, broad
O–H (carboxylic acid)	3300–2500	Strong, very broad
N–H	3500–3300	Medium, broad
C–H	3300–2700	Medium
C≡N	2260–2220	Medium
C≡C	2260–2100	Medium to weak
C=O	1780–1650	Strong
C–O	1250–1050	Strong