

# **CM1501 Tutorial/Assignment 7 & 8**

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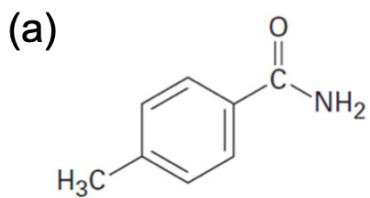
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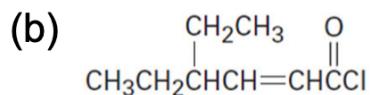
## **Tutorial 7 (Acid Derivative, Benzene, Aromatic)**

- EWG by resonance effect renders no reaction for Friedel Craft reactions, but other electrophilic substitution still occurs.

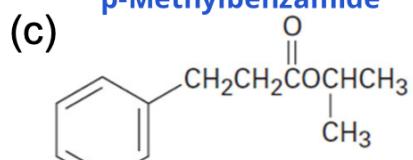
### **Nomenclature**



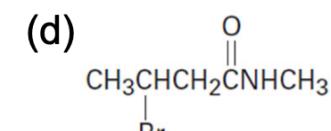
**p-Methylbenzamide**



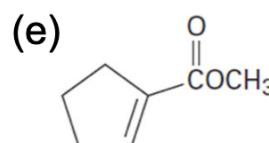
**4-Ethyl-2-hexenoyl chloride**



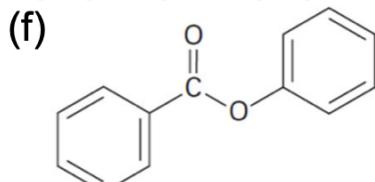
**Isopropyl 3-phenylpropanoate**



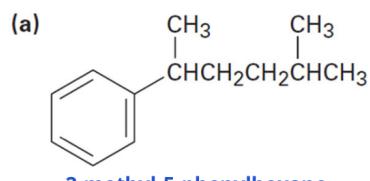
**N-Methyl-3-bromobutanamide**



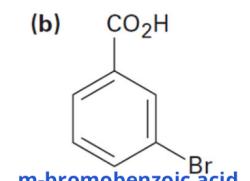
**Methyl 1-cyclopentenecarboxylate**



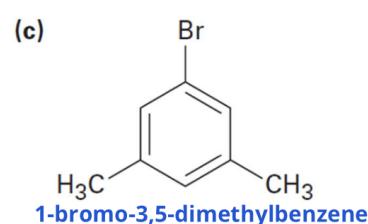
**Phenyl benzoate**



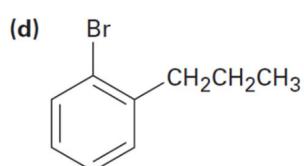
**2-methyl-5-phenylhexane**



**m-bromobenzoic acid  
or 3-bromobenzoic acid**



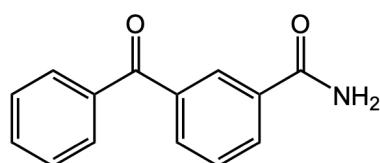
**1-bromo-3,5-dimethylbenzene**



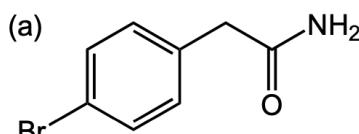
**o-bromopropylbenzene or  
1-bromo- 2-propylbenzene**



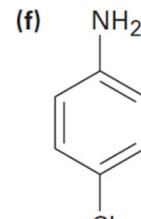
**1-fluoro-2,4-dinitrobenene**



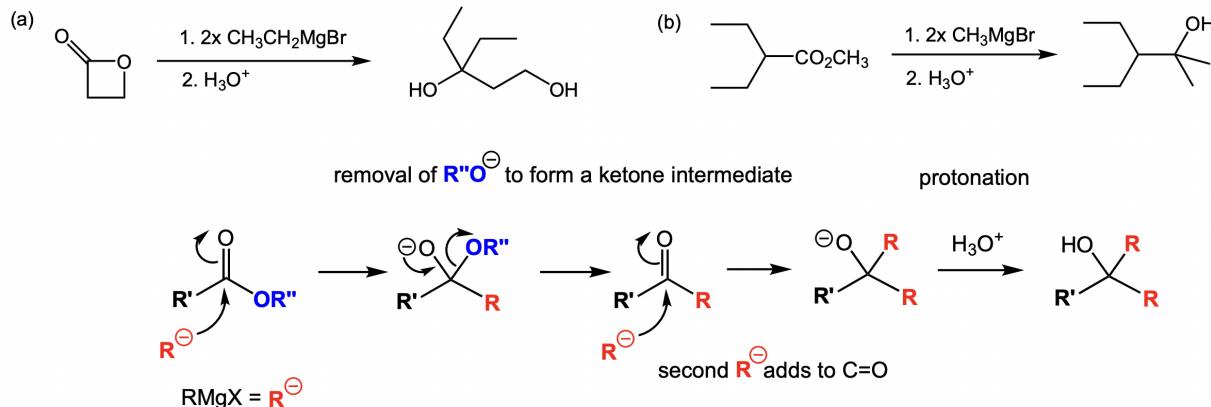
**m-Benzoylbenzamide**



**p-Bromophenylacetamide**



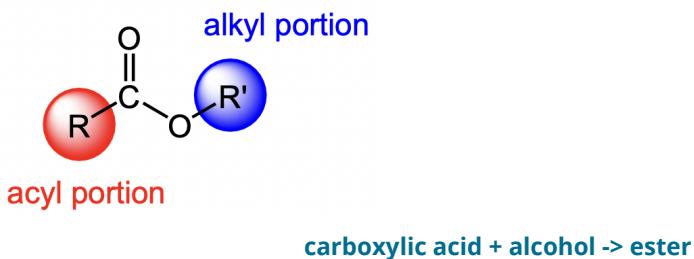
**p-chloroaniline  
or 4-chloroaniline**



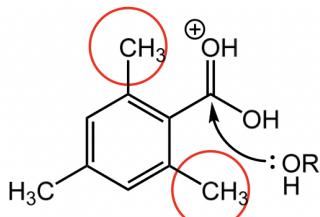
1. C=O is polarized; C of C=O is electrophilic.
  2. Grignard is strong nucleophile and adds to C=O directly.

#### ▼ Reactivity towards Saponification: ester hydrolysis in basic solution

- The reactivity of esters in saponification reactions is influenced by steric factor.
  - Branching in both the acyl and alkyl portions of an ester hinders addition of the hydroxide nucleophile.
  - This effect is less dramatic in the alkyl portion of the ester than in the acyl portion because alkyl branching is one atom farther away from the site of addition, but it is still significant.

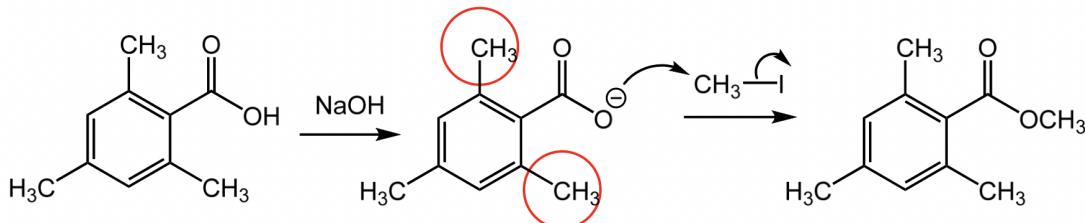


▼ Explain the observation that attempted Fischer esterification of 2,4,6-trimethylbenzoic acid with methanol and HCl is unsuccessful. No ester is obtained, and the acid is recovered unchanged. What alternative method of esterification might be successful?

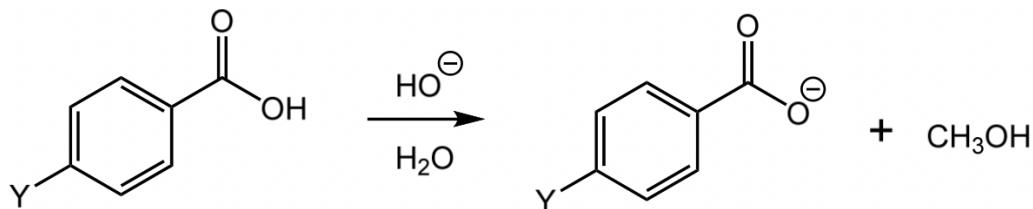


2,4,6-Trimethylbenzoic acid has two methyl groups at the ortho positions relative to the COOH group. These methyl groups hinder the approach of an alcohol ROH to add to the C=O. So the steric factor discourages the esterification process.

An alternate route is to treat the acid with NaOH to form the carboxylate ion followed by addition of  $\text{CH}_3\text{I}$ . The carboxylate ion nucleophile is one atom away from the C=O carbon, so sterically it is not as demanding. A SN2 reaction will then form the desired ester.



▼ The following reactivity order has been found for the basic hydrolysis of *p*-substituted methyl benzoates:  $\text{Y}=\text{NO}_2 > \text{Br} > \text{H} > \text{CH}_3 > \text{OCH}_3$ . How can you explain this reactivity order? Where would you expect  $\text{Y} = \text{C}\equiv\text{N}$ ,  $\text{Y} = \text{CHO}$ , and  $\text{Y} = \text{NH}_2$  to be in the reactivity list?

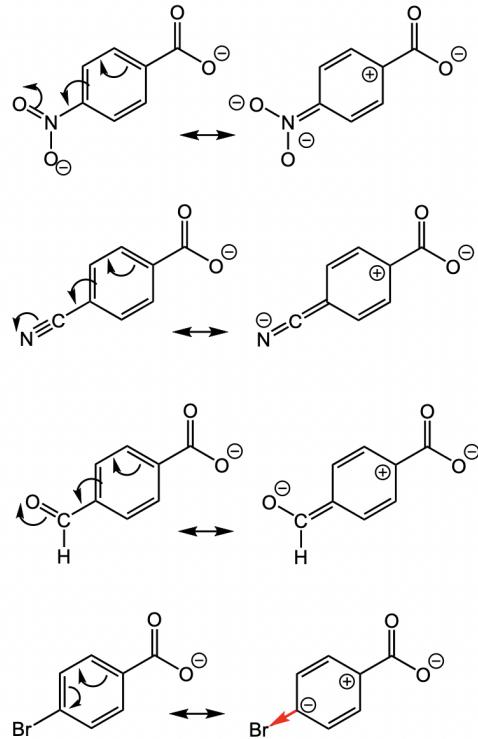


1. The reactivity order reflects the relative ease of deprotonation.
2. This also indirectly reflects the ease of formation of carboxylate anion.
3. This in turn could be explained by the relative stability of the carboxylate anion – the more stable the carboxylate anion, the faster its formation, the easier the deprotonation, the higher the reactivity order.
4. In an explanation of the reactivity order, factors that will stabilize or destabilize the carboxylate anion should be considered – mainly inductive or resonance effects; normally resonance is more effective than inductive.

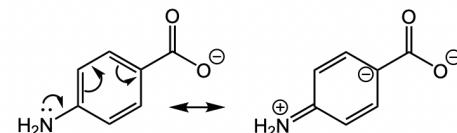
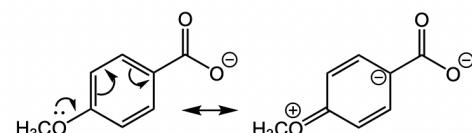
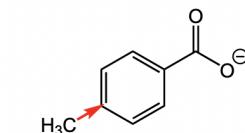
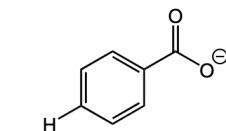
$$Y = \text{NO}_2 > \text{CN} > \text{CHO} > \text{Br} > \text{H} > \text{CH}_3 > \text{OCH}_3 > \text{NH}_2$$

- Both N and O are highly electronegative.  $\text{NO}_2$  is the strongest e-withdrawing by resonance. One resonance structure has positive charge next to carboxylate anion: a special stabilization effect.
- CN is next in line in e-withdrawing ability by resonance. It could also have resonance structure where a positive charge is next to carboxylate anion: a special stabilization effect.
- While O is more electronegative than N, the  $\text{C}\equiv\text{N}$  is more polarized because it is a C-triple bond-N. So CN offers stronger resonance effect than CHO. But CHO is also e-withdrawing, also having a resonance structure where a positive charge is next to carboxylate anion: a special stabilization effect.
- Br and C valence orbitals are mismatched, so resonance effect is weak. Bromine is relatively much less electronegative than O or N but could stabilize a negative charge next to it by inductive effect.

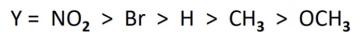
- Benzoic carboxylate is used as a reference.



- $\text{CH}_3$  group is e-donating by inductive effect (hyperconjugation). However its effect is weak, though it still somewhat intensifies the negative electron density of the carboxylate anion.
- O and C valence orbitals are matched for strong resonance effect. It is an e-donating effect. In one resonance structure, a negative charge is next to the carboxylate anion: a particularly destabilization effect.
- N lone pair is more basic than that of O. So  $\text{NH}_2$  shows the strongest e-donating resonance effect. In one resonance structure, a negative charge is next to the carboxylate anion: a particularly destabilization effect.

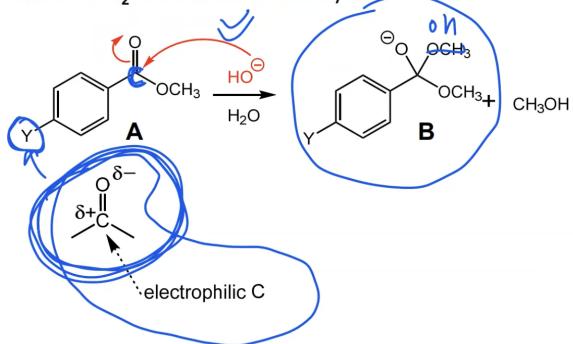


The following reactivity order has been found for the basic hydrolysis of *p*-substituted methyl benzoates:

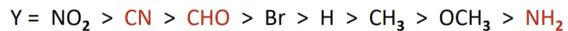


How can you explain this reactivity order?

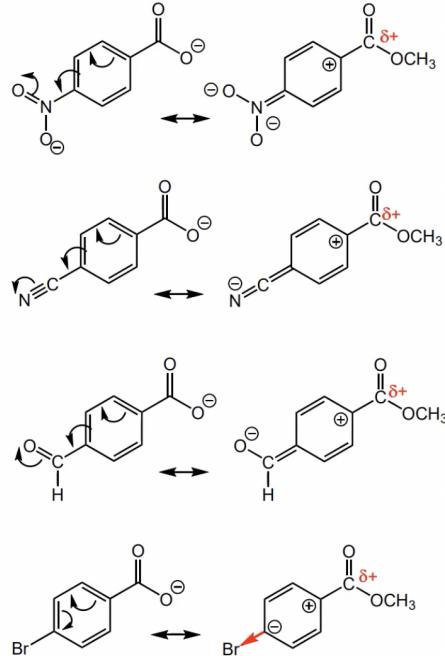
Where would you expect  $Y = \text{C}\equiv\text{N}$ ,  $Y = \text{CHO}$ , and  $Y = \text{NH}_2$  to be in the reactivity list?



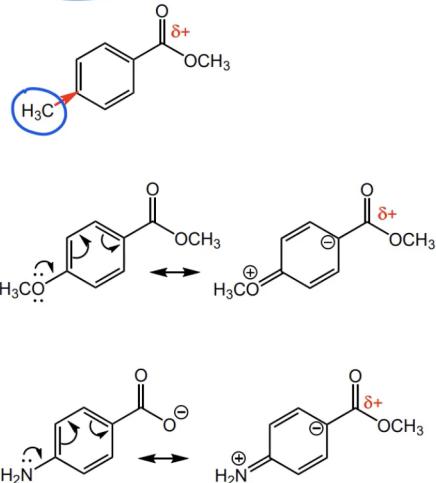
1. The reactivity order reflects the relative ease of nucleophilic addition of  $\text{HO}^-$  to the  $\text{C=O}$ .
2. This also indirectly reflects the relative electrophilicity of the  $\text{C=O}$  carbon in A.
3. This in turn could be explained by the relative e-deficiency in A – the more electrophilic the  $\text{C=O}$  carbon in A, the faster the  $\text{HO}^-$  addition, the higher the reactivity order to form B.
4. In an explanation of the reactivity order, factors that will intensify the electrophilicity of the  $\text{C=O}$  carbon in A should be considered – mainly inductive or resonance effects; normally resonance is more effective than inductive.



- Both N and O are highly electronegative.  $\text{NO}_2$  is the strongest e-withdrawing by resonance. One resonance structure has positive charge next to  $\text{C=O}$  carbon  $\delta+$ : intensifying the C electrophilicity.
- CN is next in line in e-withdrawing ability by resonance. It could also have resonance structure where a positive charge is next to  $\text{C=O}$  carbon  $\delta+$ : intensifying the C electrophilicity.
- While O is more electronegative than N, the  $\text{C}\equiv\text{N}$  is more polarized because it is a C-triple bond-N. So CN offers stronger resonance effect than CHO. But CHO is also e-withdrawing, also having a resonance structure where a positive charge is next to  $\text{C=O}$  carbon  $\delta+$ : intensifying the C electrophilicity.
- Br and C valence orbitals are mismatched, so resonance effect is weak. Bromine is relatively much less electronegative than O or N but could intensity the electrophilicity of the  $\text{C=O}$  carbon  $\delta+$  by inductive effect.

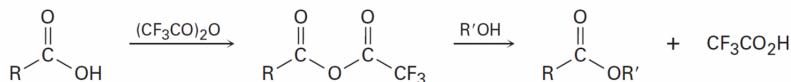


- CH<sub>3</sub> group is e-donating by inductive effect (hyperconjugation). Its effect is weak but it still somewhat helps stabilize the electrophilic C=O carbon δ+.

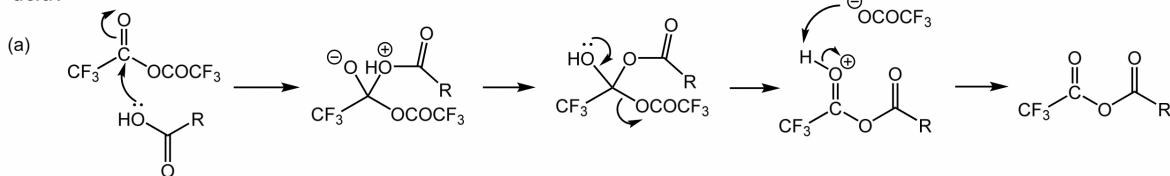


- O and C valence orbitals are matched for strong resonance effect. It is an e-donating effect. In one resonance structure, a negative charge is next to the **electrophilic C=O carbon δ+**: a particularly **good** stabilization effect.
- N lone pair is more basic than that of O. So NH<sub>2</sub> shows the strongest e-donating resonance effect. In one resonance structure, a negative charge is next to the **electrophilic C=O carbon δ+**: a particularly **strong** stabilization effect.

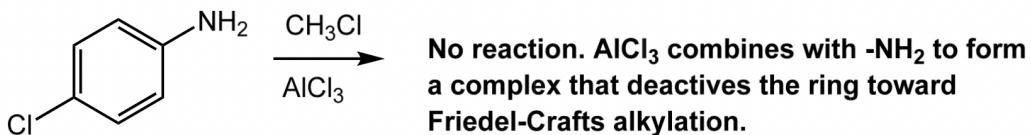
Treatment of a carboxylic acid with trifluoroacetic anhydride leads to an unsymmetrical anhydride that rapidly reacts with alcohol to give an ester.

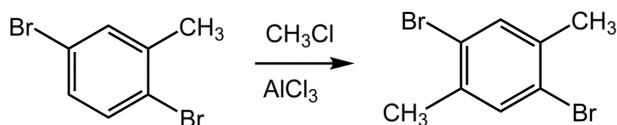


- Propose a mechanism for formation of the unsymmetrical anhydride.
- Why is the unsymmetrical anhydride unusually reactive?
- Why does the unsymmetrical anhydride react as indicated rather than giving a trifluoroacetate ester plus carboxylic acid?



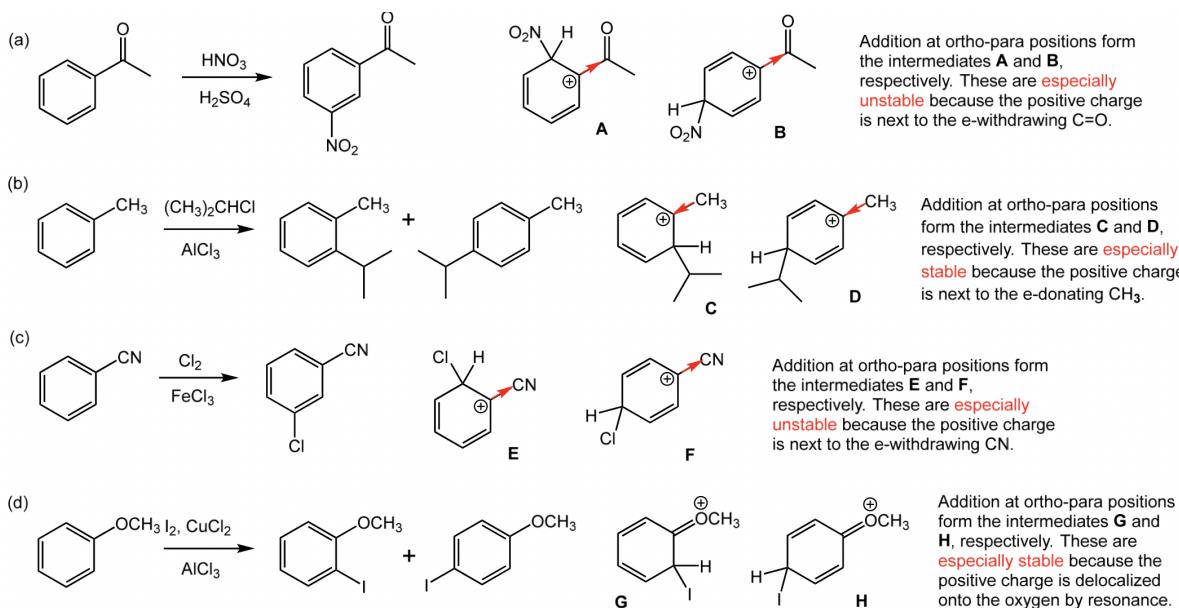
- The CF<sub>3</sub> groups are strongly e-withdrawing due to high electronegativity of F. So the C=O is highly polarized, and the carbon is highly electrophilic. Even a weak nucleophile COOH lone pair could add to the C=O as indicated in (a).
- The trifluoroacetate anion, CF<sub>3</sub>COO<sup>-</sup>, is a very good leaving group due to e-withdrawing CF<sub>3</sub> group.



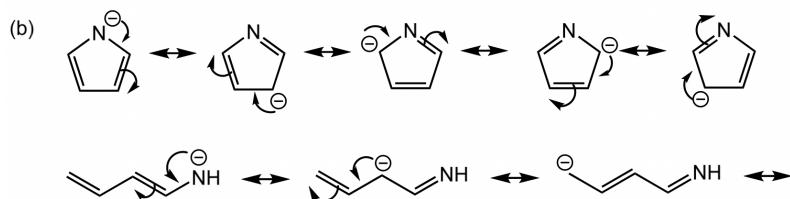
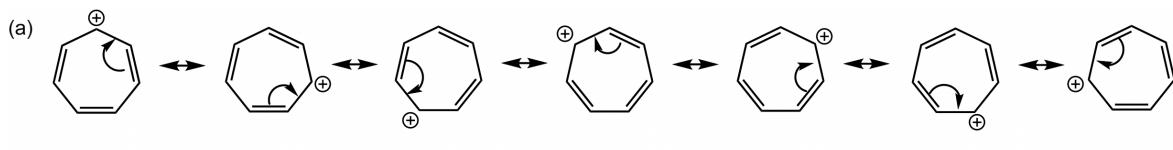


1. Alkylation occurs in the indicated position because the methyl group is more activating than bromine, and
2. Because substitution rarely takes place between two substituents (steric effect).

▼ Predict the product(s) for each reaction below. In each case, draw the resonance forms of the intermediate to explain the observed regiochemistry.

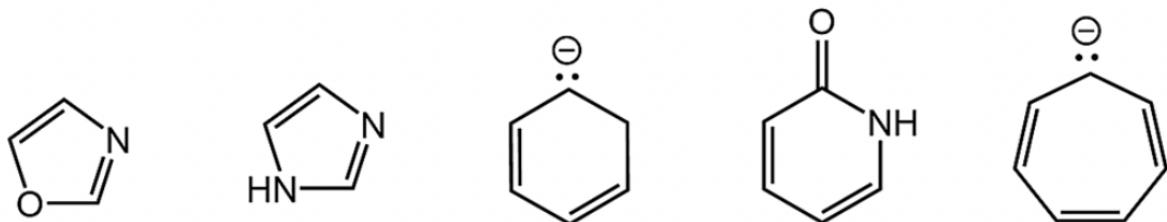


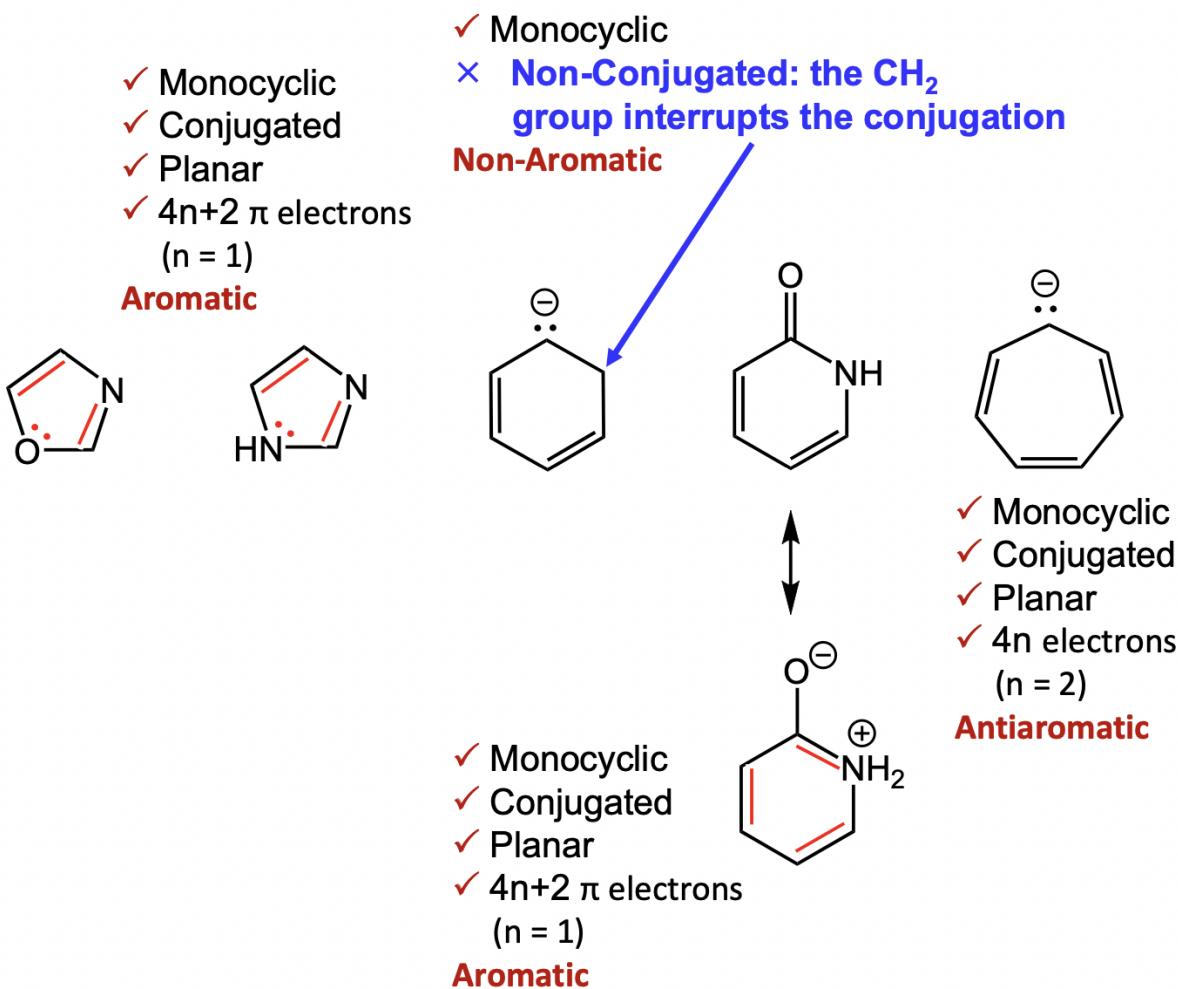
▼ Consider the aromatic anions below and their linear counterparts. Draw all of the resonance forms for each. What patterns emerge?



In the cyclic compounds, the charge could be placed on every atom in the ring, while in the linear compounds the charge could only reside on every other atom.

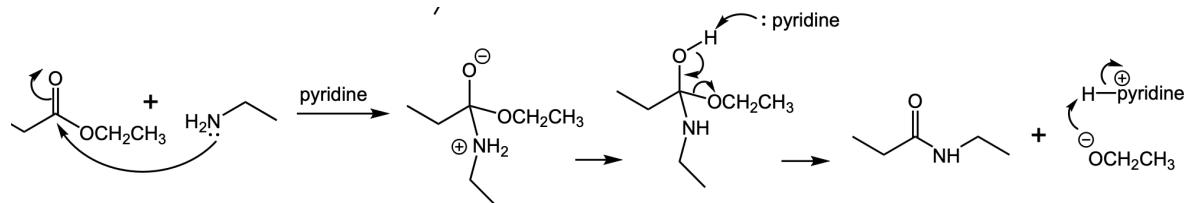
▼ How many of the following compounds are aromatic?



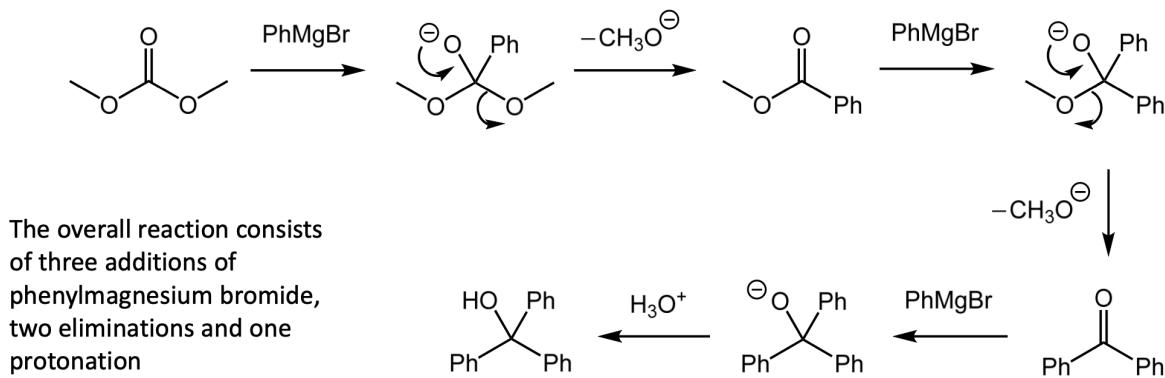


## Assignment 7

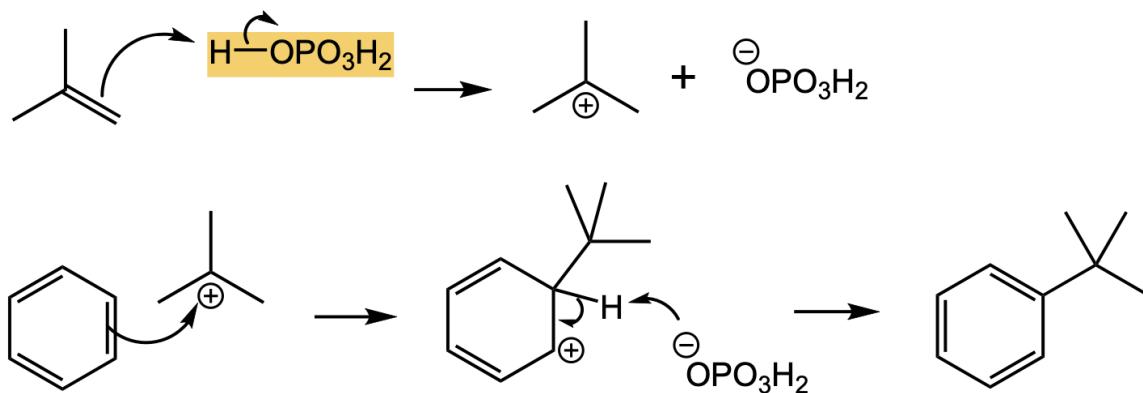
▼ Ester + amine with pyridine reaction



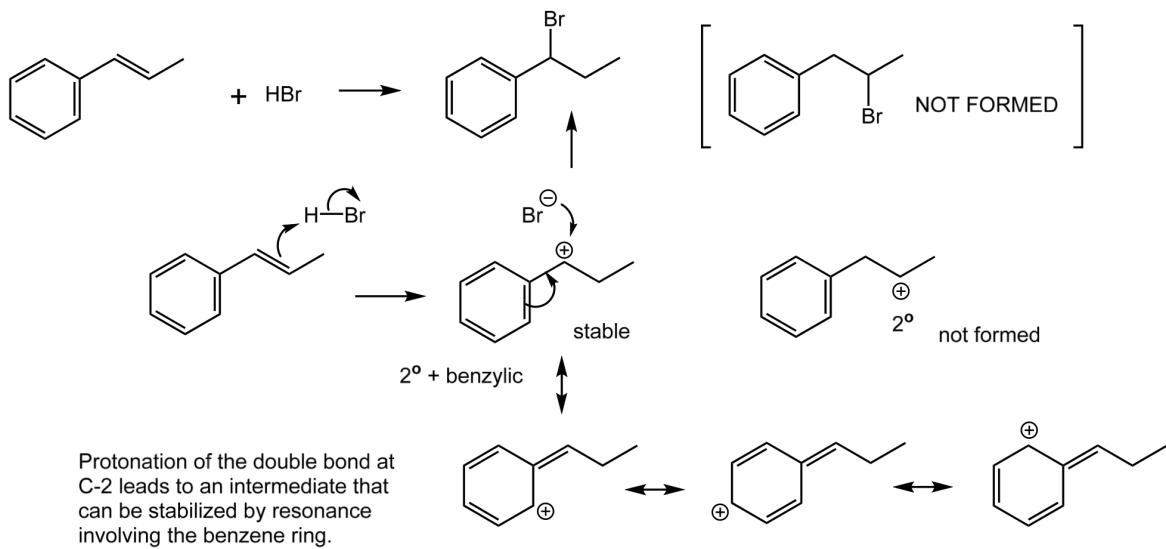
▼ Grignard reaction of an excess of phenylmagnesium bromide with dimethyl carbonate,  $\text{CH}_3\text{OCO}_2\text{CH}_3$



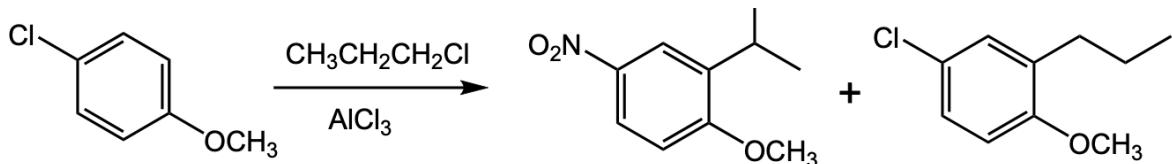
▼ The carbocation electrophile in a Friedel-Crafts reaction can be generated by an alternate means than reaction of an alkyl chloride with AlCl<sub>3</sub>. For example, reaction of benzene with 2-methylpropene in the presence of H<sub>3</sub>PO<sub>4</sub> yields *t*-butylbenzene. Propose a mechanism for this reaction.



▼ Regioselectivity of electrophilic addition:  
Addition of HBr to 1-phenylpropene yields only (1-bromopropyl)benzene.  
Propose a mechanism for the reaction and explain why none of the other regioisomer is produced.



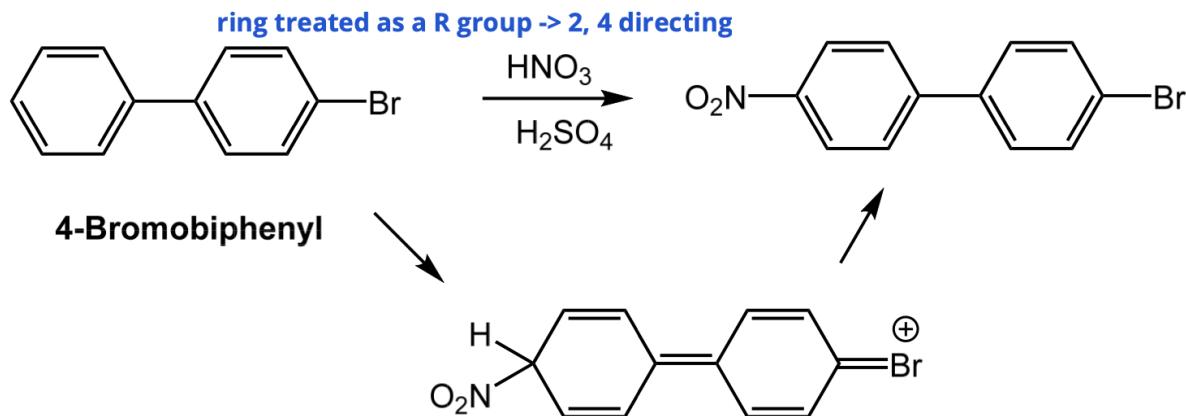
▼ Note rearrangement in forming carbocation intermediates.



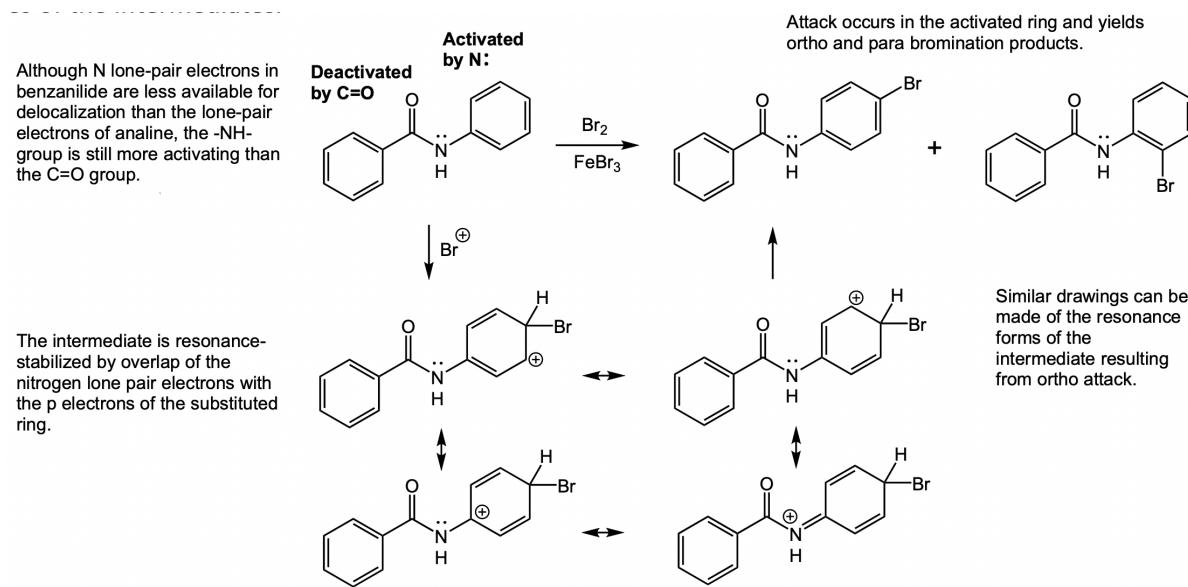
Orientation is directed by the stronger activating  $\text{OCH}_3$  group; rearranged and un-rearranged side chains are present in the products.

▼ At what position and on what ring do you expect nitration of 4-bromobiphenyl to occur? Explain, using resonance structures of the potential intermediates.

- attack occurs on the unsubstituted ring because Br is deactivating.
- attack occurs on the p position of the ring because the positively charged intermediate can be stabilised by resonance contributions from Br

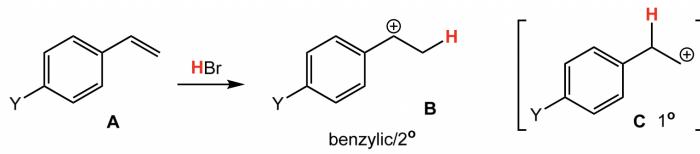


▼ At what position, and on what ring, would you expect bromination of benzanimide to occur? Explain by drawing resonance structures of the intermediates.



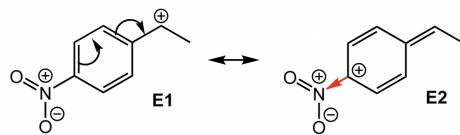
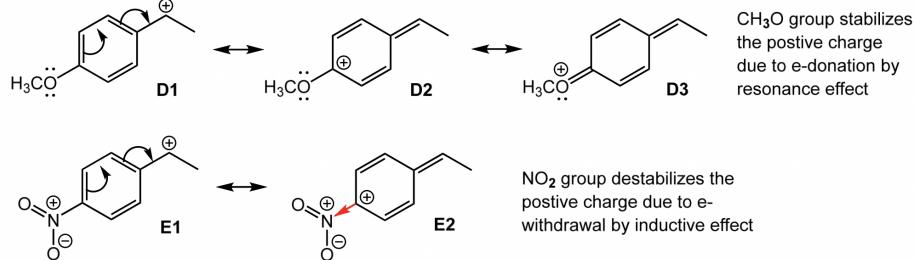
▼ Predict which of the following two alkenes reacts faster with HBr. Explain your answer by drawing resonance structures of the carbocation intermediates.

1. In the first protonation step, **B** is strongly preferred because it is significantly more stable than **C**.

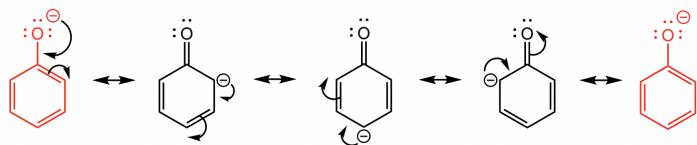


2. If Y stabilizes the positive charge in **B**, it is going to be formed faster, thus the faster the HBr addition.

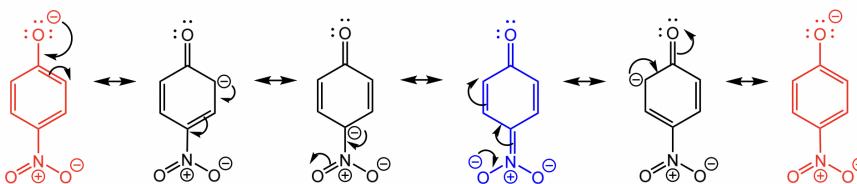
3. If Y destabilizes the positive charge in **B**, it is going to be formed slower, thus the slower the HBr addition.



▼ Phenols (ArOH) are relatively acidic, and the presence of a substituent group on the aromatic ring has a large effect. The pKa of unsubstituted phenol is 9.89, while that of *p*-nitrophenol is 7.15. Draw resonance structures of the corresponding phenoxide anions and explain the data.

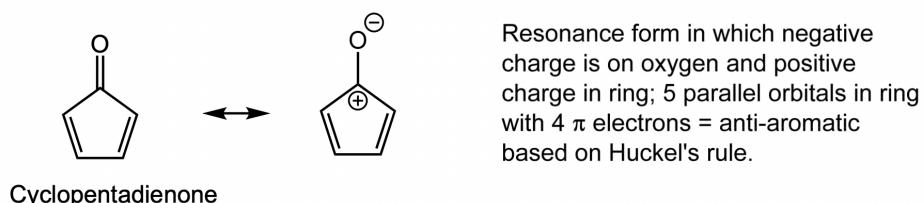
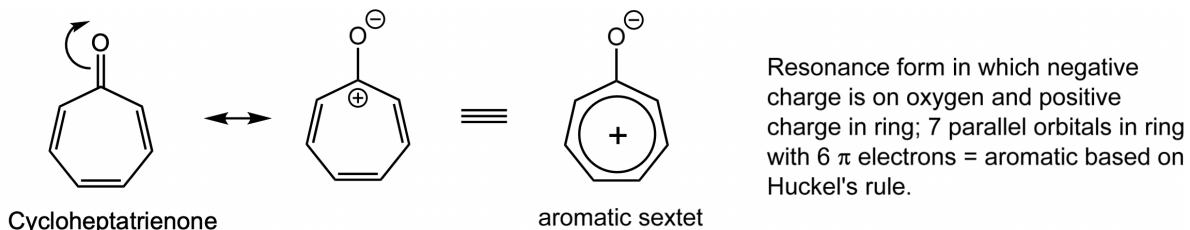


An e-withdrawing substituent stabilizes a negatively charged intermediate. An NO<sub>2</sub> group stabilizes the phenoxide anion by resonance (as shown in the blue resonance structure)



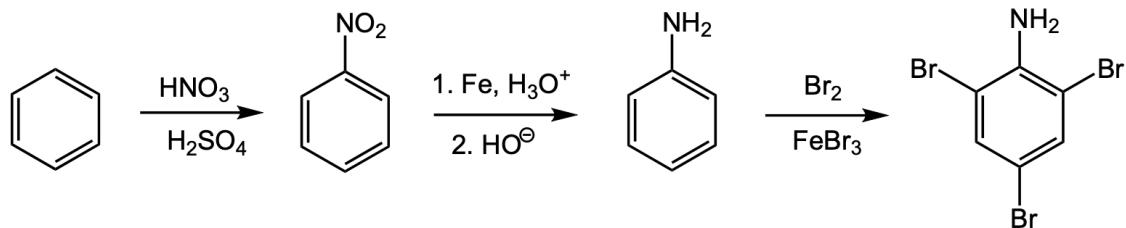
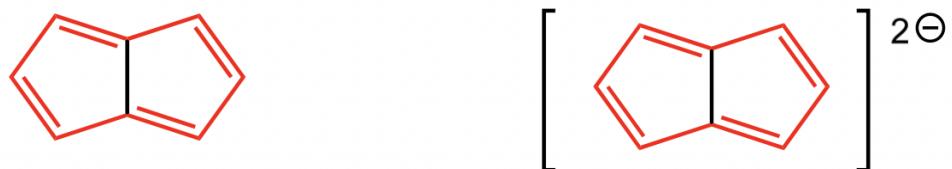
where the negative charge is delocalized onto the oxygen of the NO<sub>2</sub> group so it is formed more readily. Thus the dissociation is greater to make the *p*-nitrophenol more acidic, giving a lower pKa value.

▼ Cycloheptatrienone is stable, but cyclopentadienone is so reactive that it can't be isolated. Explain, taking the polarity of the carbonyl group into account.



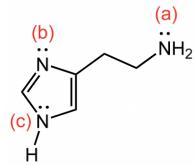
▼ Pentalene is a most elusive molecule that has been isolated only at liquid-nitrogen temperature. The pentalene dianion, however, is well known and quite stable. Explain.

- Pentalene has  $8\pi$  electrons ( $4n$ ,  $n=2$ ) and is antiaromatic.
- Pentalene dianion, however has  $10\pi$  electrons ( $4n+2$ ,  $n=2$ ) and is a stable, aromatic ion.
- Both are planar.
- Both have a peripheral monocyclic, conjugated system (in red) with 8p orbitals.



# Tutorial 8 (Amines, Macromolecules, Spectroscopy)

- ▼ Histamine, whose release in the body triggers nasal secretions and constricted airways, has three nitrogen atoms. List them in order of increasing basicity and explain your ordering.



- (a) Most basic N. The lone pair is in a  $\text{sp}^3$  orbital that is most available to Lewis acids.
- (b) Less basic than that in (a). The lone pair is in a  $\text{sp}^2$  orbital that is closer to nucleus, thus relatively less available to Lewis acids.
- (c) Least basic. The lone-pair electrons are part of the ring's aromatic 6-p electron system.

- ▼ Account for the fact that *p*-nitroaniline ( $\text{pK}_a$  5.1.0) is less basic than *m*-nitroaniline ( $\text{pK}_a$  5.2.5) by a factor of 30. Draw resonance structures to support your argument. (The  $\text{pK}_a$  values refer to the corresponding ammonium ions.)



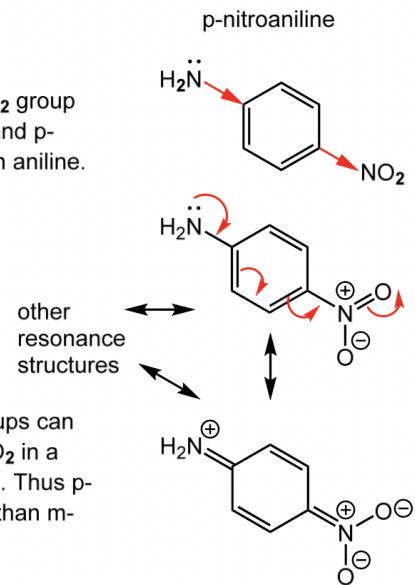
INDUCTIVE EFFECT:

The inductive effect of the e-withdrawing  $\text{NO}_2$  group makes the lone-pairs of both m-nitroaniline and p-nitroaniline less available and less basic than aniline.

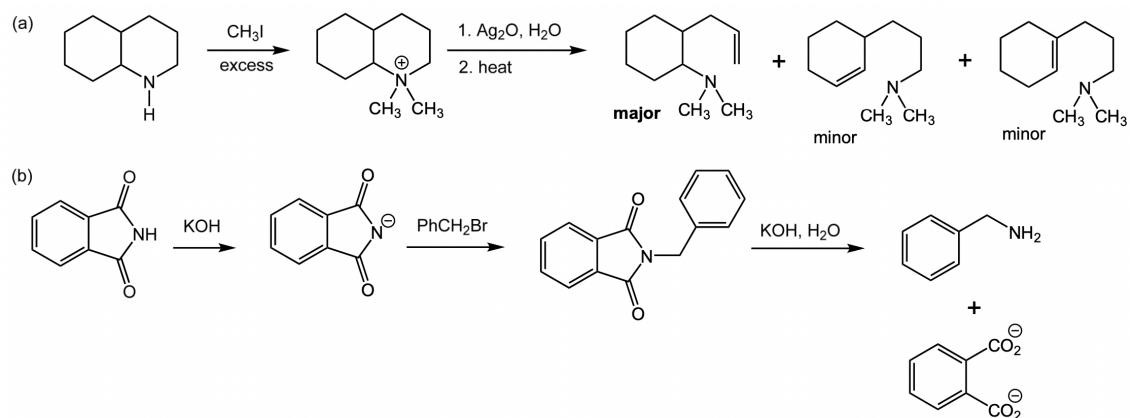
no resonance effect

RESONANCE EFFECT:

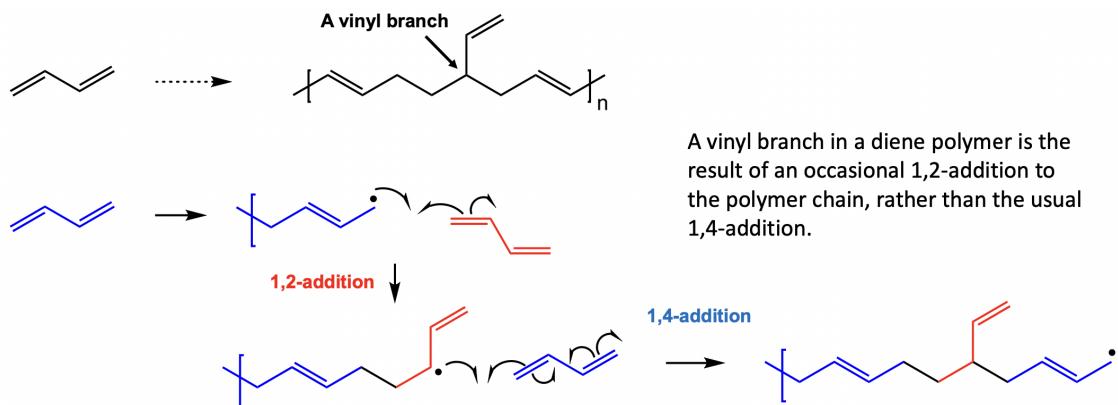
Conjugation of the  $\text{NH}_2$  and  $\text{NO}_2$  groups can delocalize the lone pair on  $\text{NH}_2$  to  $\text{NO}_2$  in a especially stable resonance structure. Thus p-nitroaniline is significantly less basic than m-nitroaniline and aniline.



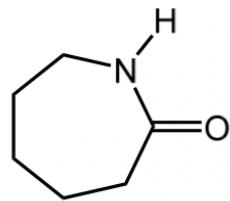
▼ Predict the product(s) of the following reactions. If more than one product is formed, tell which is major.



▼ Diene polymers contain occasional vinyl branches along the chain. How do you think these branches might arise?

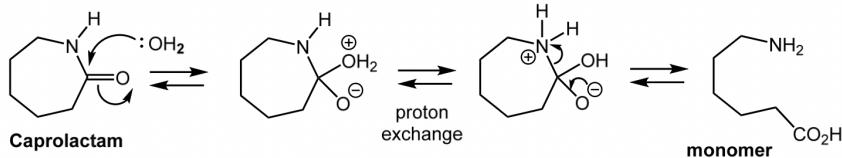


▼ The step-growth polymer nylon 6 is prepared from caprolactam. The reaction involves initial reaction of caprolactam with water to give an intermediate open-chain amino acid, followed by heating to form the polymer. Propose mechanisms for both steps and show the structure of nylon 6.

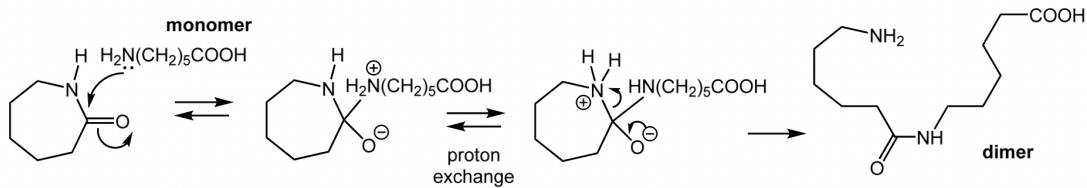


**Caprolactam**

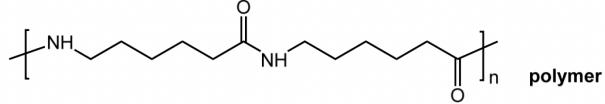
**Step 1:** water opens the caprolactam ring to form the amino acid intermediate **monomer**.



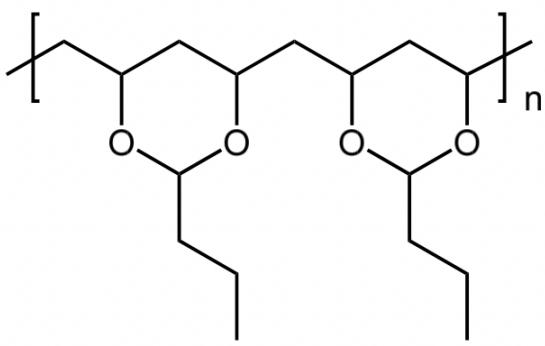
**Step 2:** Reaction of the **monomer** with a second molecule of caprolactam forms a **dimer**.



**Step 3** and beyond: Reaction of the dimer with caprolactam repeats itself many, many times until the polymer stops growing. Heat will favor in the equilibrium in the direction of the polymer formation.

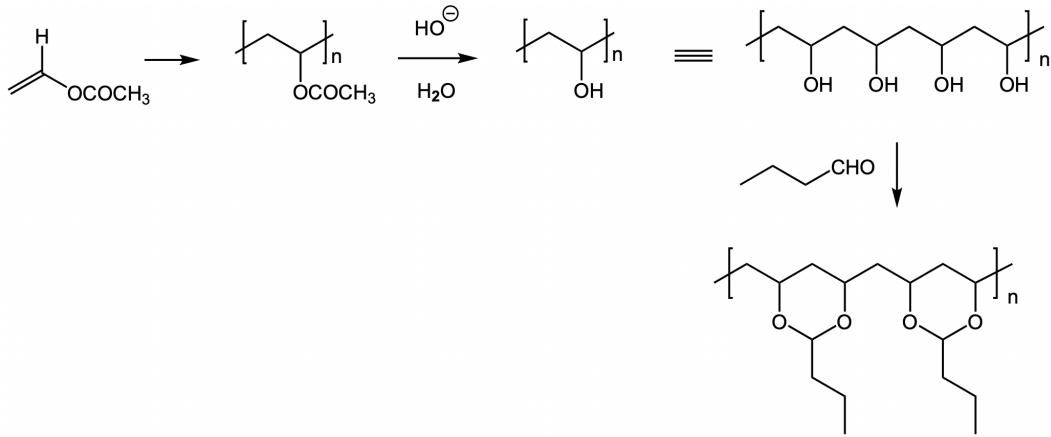
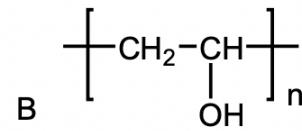
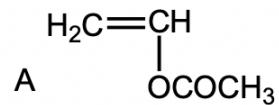


▼ **Poly(vinyl butyral)** is used as the plastic laminate in the preparation of automobile windshield safety glass. How would you synthesise this polymer?



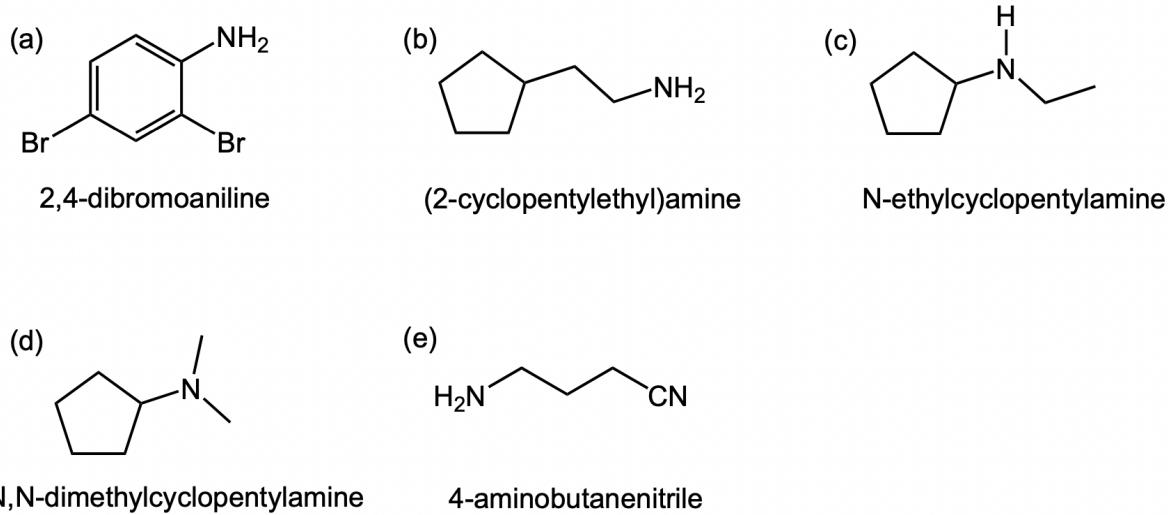
**Poly(vinyl butyral)**

HINT: use the following monomer A to prepare the polymer precursor B:

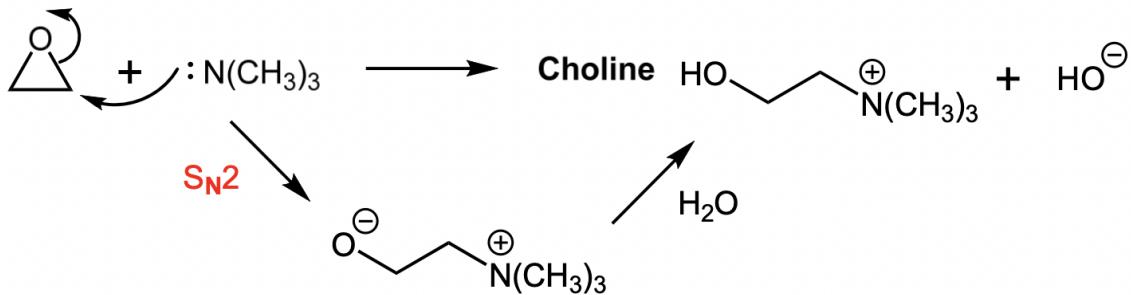


## Assignment 8

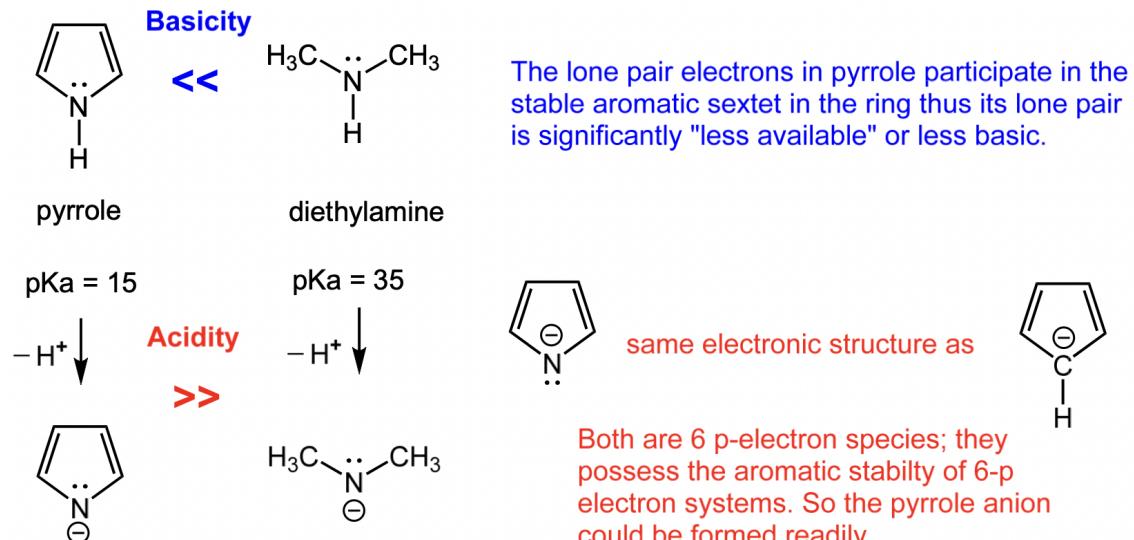
### Nomenclature



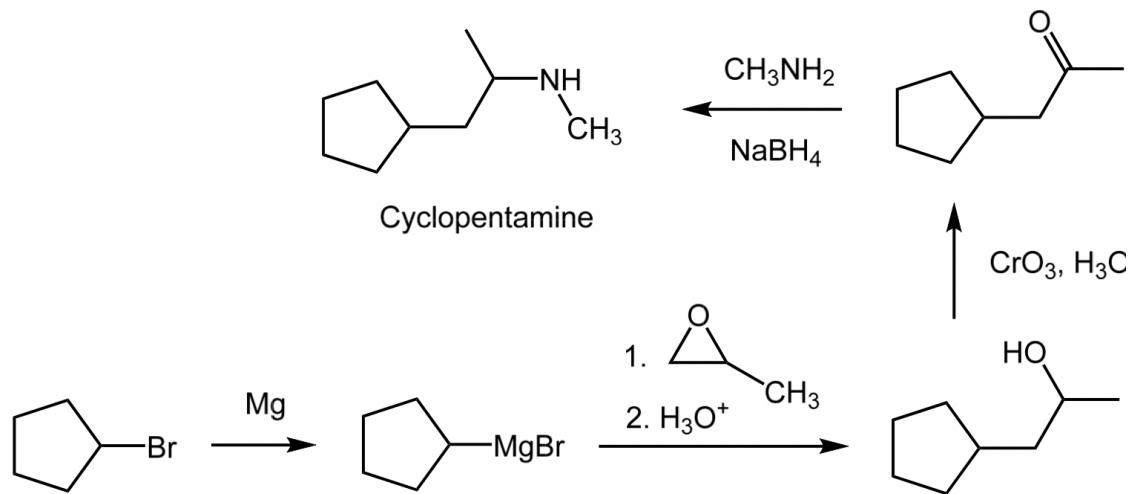
▼ Epoxide + amine reaction: Choline, a component of the phospholipids in cell membranes, can be prepared by SN2 reaction of trimethylamine with ethylene oxide in an aqueous medium. Show the structure of choline, and propose a mechanism for the reaction.



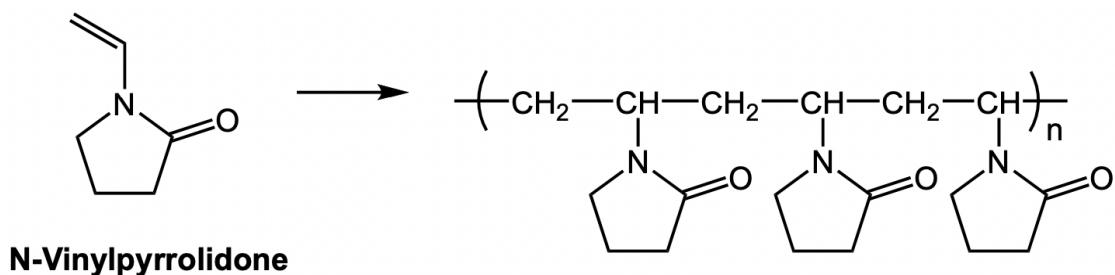
▼ Although pyrrole is a much weaker base than most other amines, it is a much stronger acid ( $pK_a \approx 15$  for the pyrrole v.s. 35 for diethylamine). The N–H proton is readily abstracted by base to yield the pyrrole anion,  $\text{C}_4\text{H}_4\text{N}^2-$ . Explain.



▼ Propose a synthesis of cyclopentamine from materials of five carbons or less.

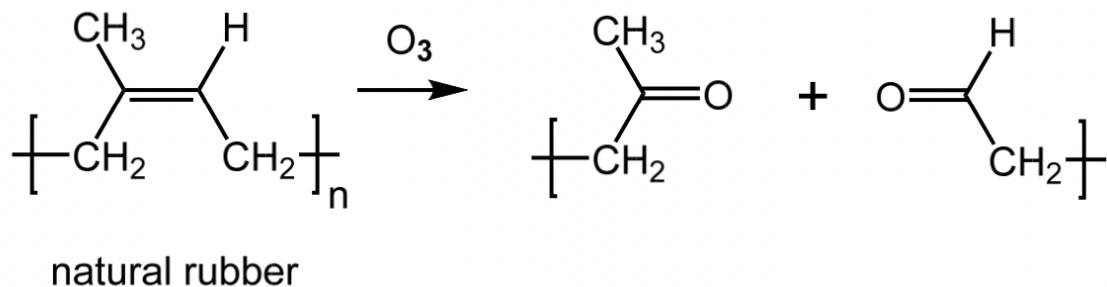


▼ Poly(vinyl pyrrolidone), prepared from *N*-vinylpyrrolidone, is used both in cosmetics and as a synthetic substitute for blood. Draw a representative segment of the polymer.

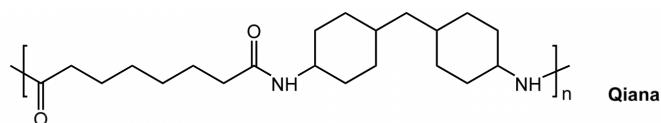


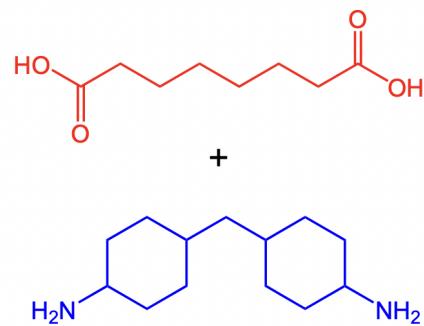
▼ Tires whose sidewalls are made of natural rubber tend to crack and weather rapidly in areas around cities where high levels of ozone and other industrial pollutants are found. Explain.

- Ozone causes oxidative cleavage of the double bond in rubber and breakers the polymer chain

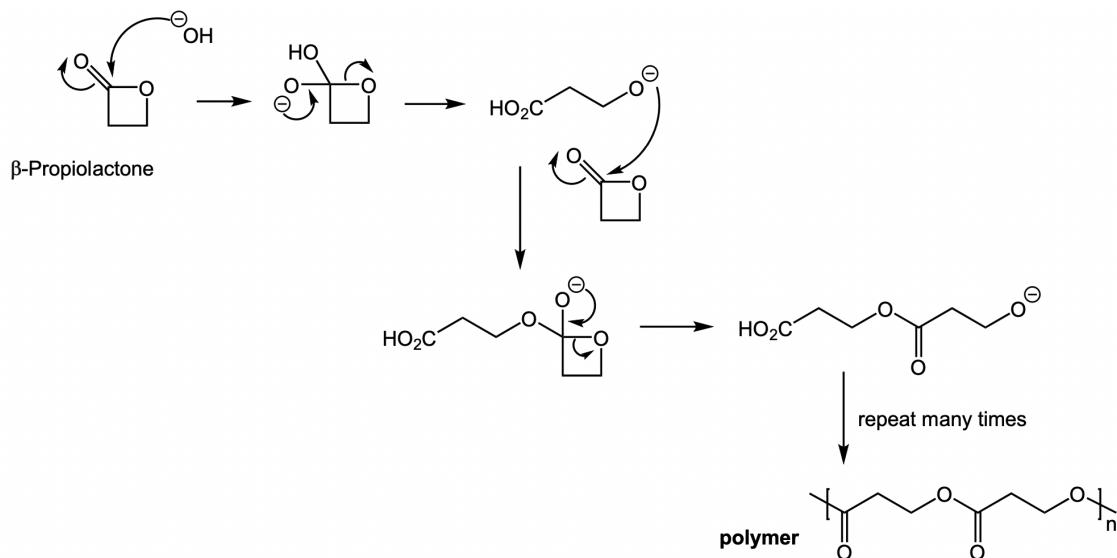


▼ *Qiana*, a polyamide fiber with a silky texture, has the following structure. Monomers?

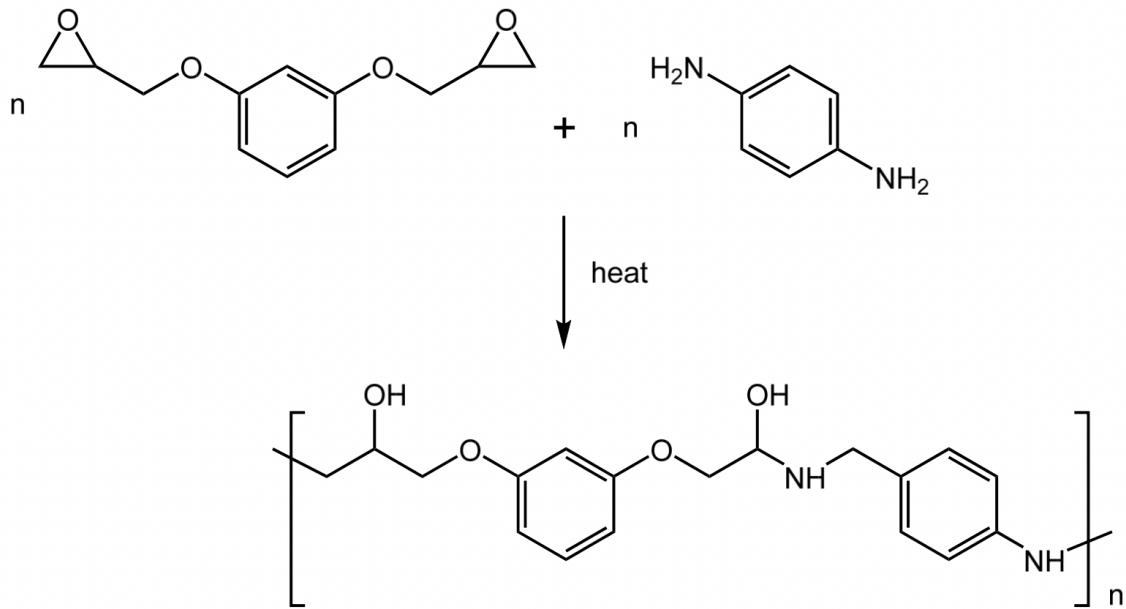




▼ What is the structure of the polymer produced by treatment of  $\beta$ -propiolactone with a small amount of hydroxide ion?



▼ Show the structure of the polymer that results from heating the following diepoxyde and diamine

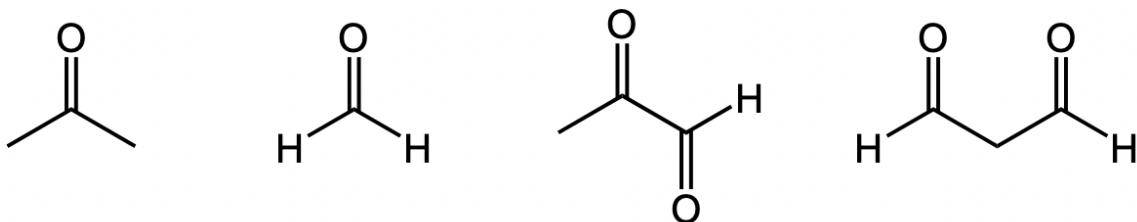


▼ How many of the following statements is/are not true?

- Natural rubber has the E-configuration throughout the polymer skeleton.
  - **False.** Natural rubber has the Z-configuration throughout the polymer skeleton.
- Natural rubber is a 1,4-addition polymer of isoprene.
  - **True**
- Natural rubber is more stretchable than its counterpart, Gutta-percha, because its polymer chains are more regular.
  - **False.** The unusual ability of natural rubber to stretch and then contract to its original shape is due to the irregular structure of the polymer chains caused by the Z-double bonds.
- In vulcanization, the formation of sulfur bridges between different chains make natural rubber harder and stronger.
  - **True.** Vulcanization cross-links the rubber chains by forming C-S bonds between them, thereby hardening and stiffening the polymer.



$\beta$ -Ocimene has the molecular formula C<sub>10</sub>H<sub>16</sub> and a UV absorption maximum at 232 nm. On hydrogenation with a palladium catalyst, 2,6-dimethyloctane is obtained. Ozonolysis of  $\beta$ -ocimene, followed by treatment with zinc and acetic acid, produces the following four fragments:



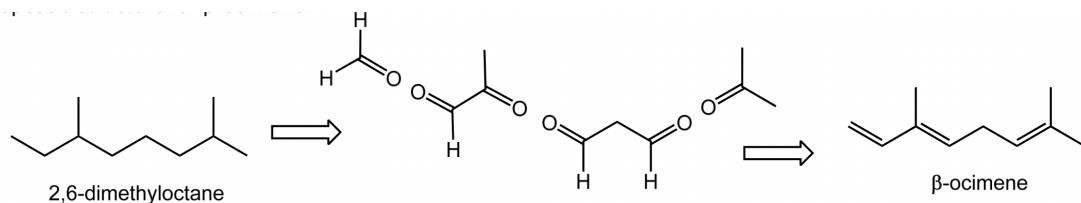
▼ How many double bonds?

- 3 IHD
- 2,6-dimethyloctane is C<sub>10</sub>H<sub>22</sub> with zero-degree unsaturation  $\rightarrow$  3 moles of hydrogen are absorbed in hydrogenation,
- i.e.  $\beta$ -ocimene has 3 double bonds and no ring.

▼ Conjugated?

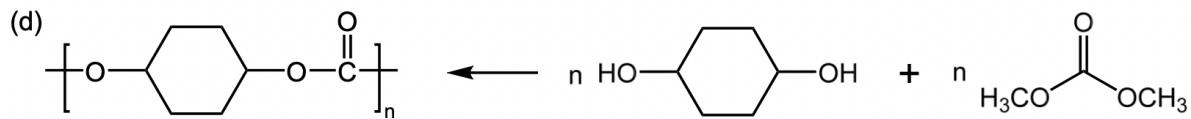
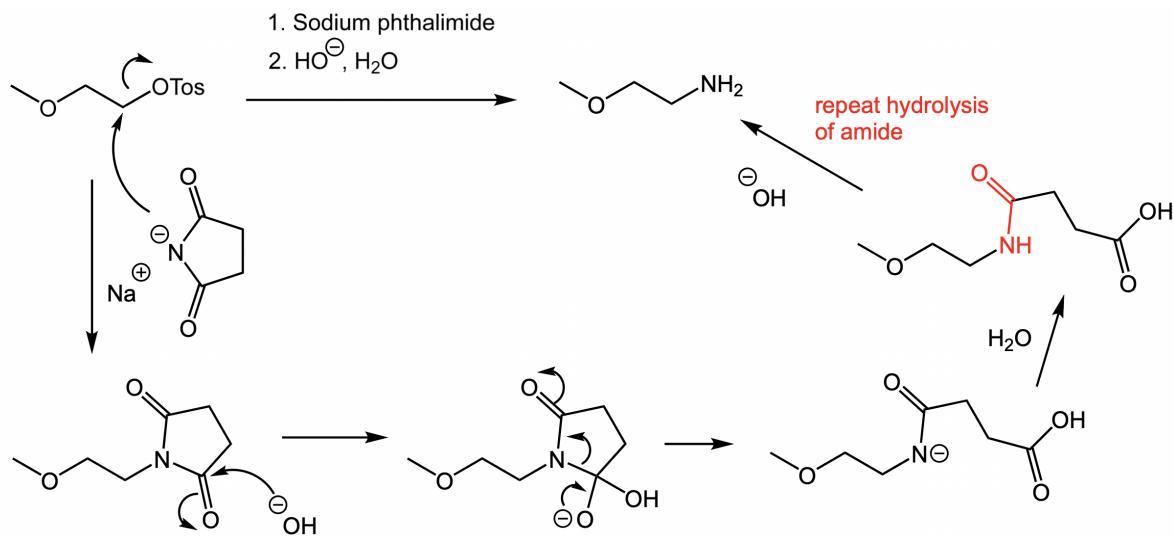
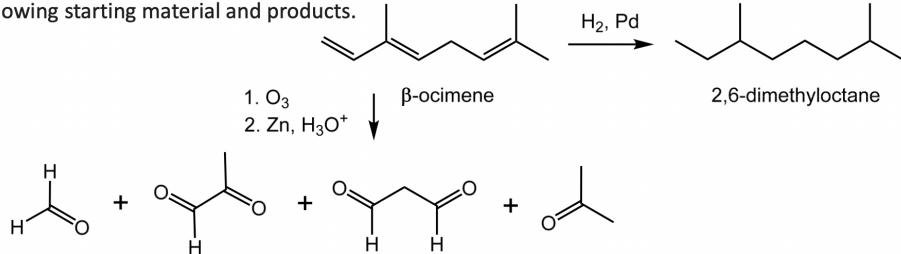
- $\lambda_{\text{max}}$  is at 232 nm, significantly longer wavelength than  $\pi \rightarrow \pi^*$  in isolated C=C (<200 nm); so  $\beta$ -ocimene is conjugated.

▼ Structure?



▼ Reactions?

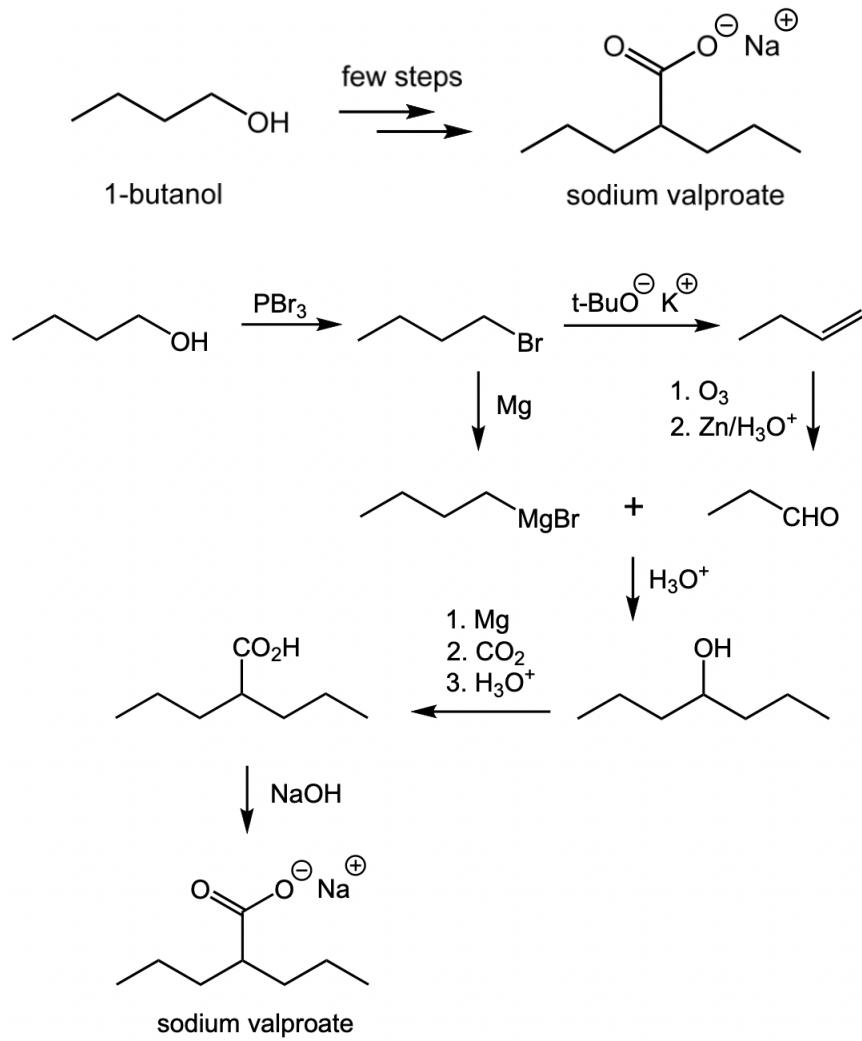
Write the reactions, showing starting material and products.



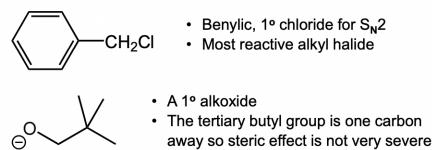
## 17/18 Final

- ▼ Sodium valproate; made from the corresponding carboxylic acid and NaOH, is used in the treatment of epilepsy. Propose a synthesis of this compound from 1-butanol.

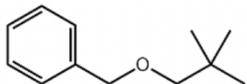
You may use any additional organic and inorganic reagents; the organic compounds used must not contain more than THREE carbon atoms.



## 19/20 Final

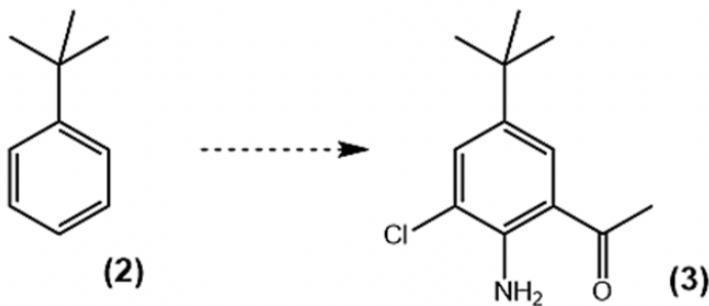


Which reaction scheme would you use to prepare benzyl neopentyl ether?

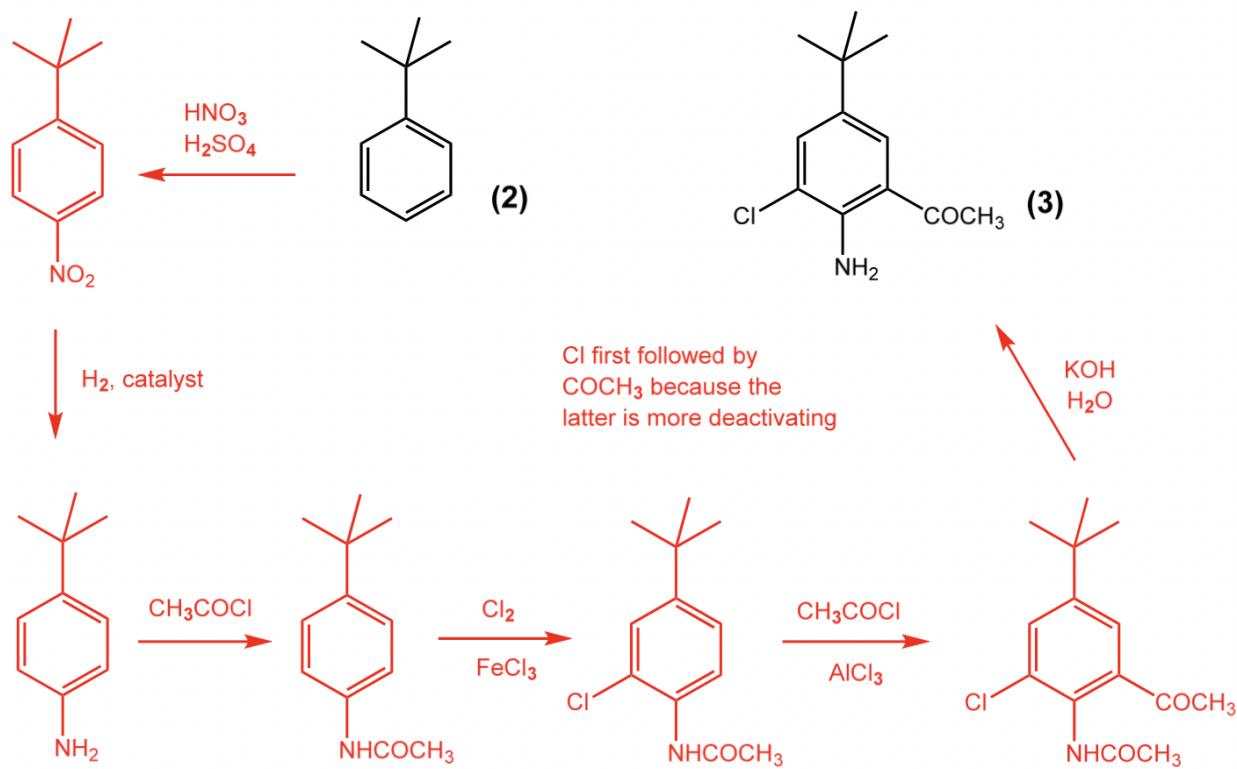


- (A)
- (B)
- (C)
- (D)

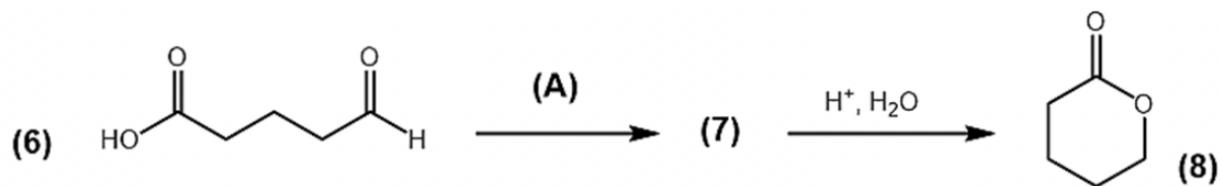
Illustrate how you could convert compound (2) to compound (3). You may use any organic and inorganic reagents.



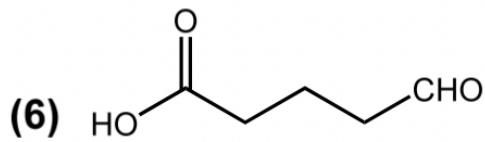
(8 marks)



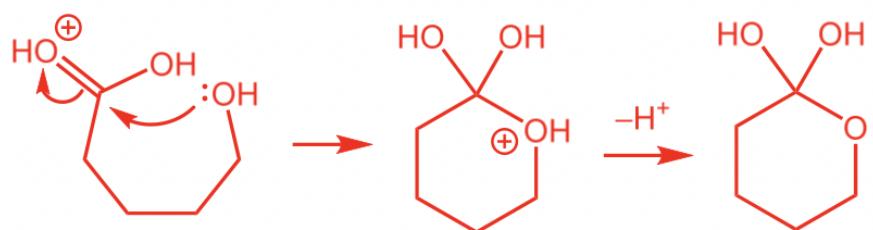
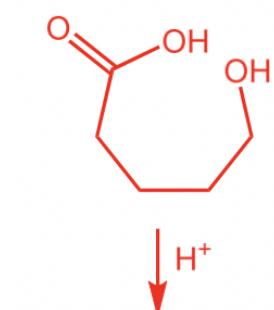
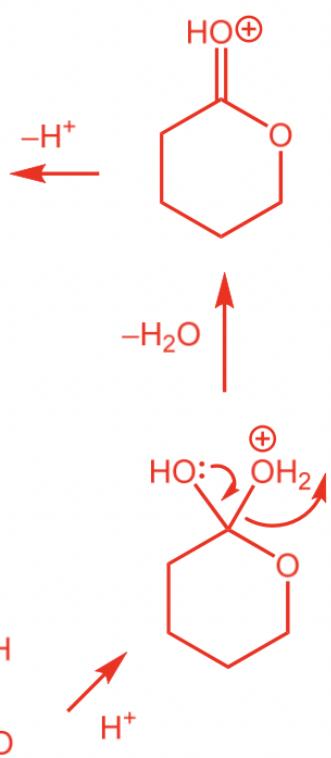
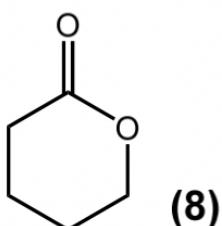
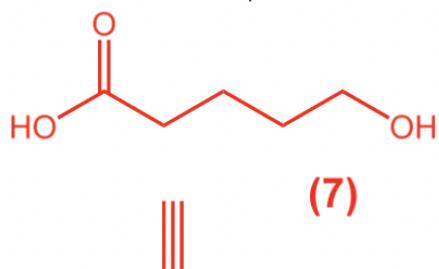
Compound (6) is converted to compound (8) via compound (7).



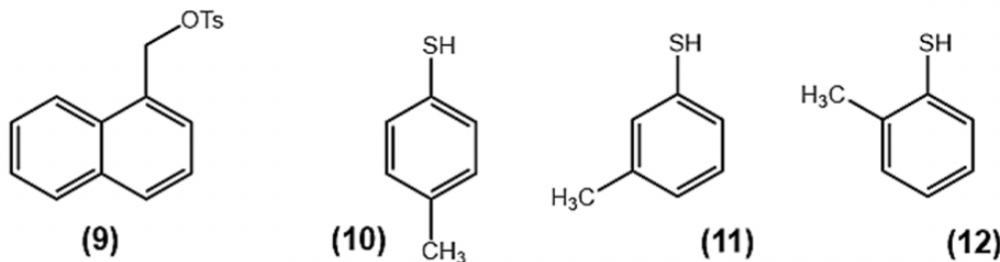
- What could be the appropriate structures for reagent (A) and compound (7), respectively.
- Provide a mechanism for the conversion of compound (7) to compound (8).



(A) =   
 1.  $\text{NaBH}_4$   
 2.  $\text{H}_3\text{O}^+$

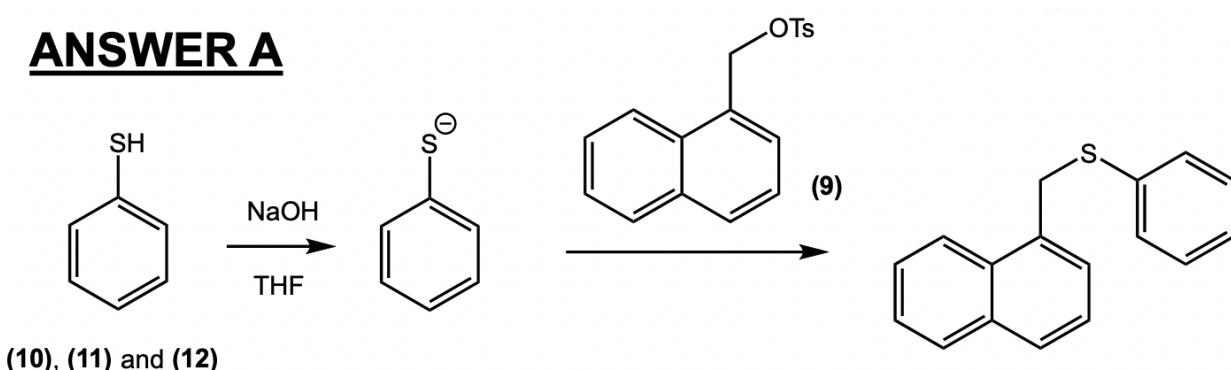


Compound (9) is used as a common substrate for the following reactions. Each of (10), (11) and (12) is treated with NaOH in THF in separate reaction flasks. Compound (9) is added to each of the flasks and the reactions are carried out under identical conditions. Three different products are obtained, respectively. Two of the products are isolated in 80-85% yield. One product is, however, isolated in 40-45% yield.



- Which of the three reactions gives the product in lower yield? Explain.
- In the reaction selected in (a), changing the solvent to methanol further decreases the yield to 20-25%. Explain

## **ANSWER A**

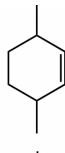
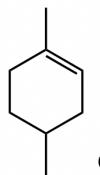
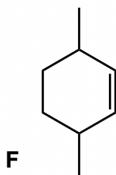


(10), (11) and (12)

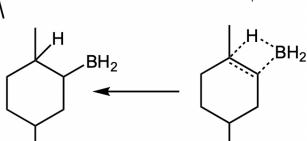
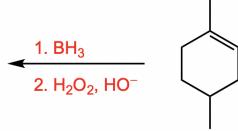
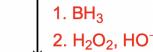
1.  $\text{--SH}$  reacts with  $\text{HO}^-$  to form  $\text{--S}^-$  anion: a strong nucleophile favoring SN2
  2. THF is a mildly polar aprotic solvent: a good solvent for SN2
1. The reaction between (9) and (12) will be the slowest. All three reactions go through SN2, and STERIC FACTOR is the main consideration. The substrate (9) is a primary tosylate BUT the aromatic ring is large and imposes steric hindrance to incoming nucleophiles. Compound (12) is ortho-disubstituted, so the  $\text{--S}^-$  anion from (12) is the sterically most bulky nucleophile due to the ortho-methyl group present. The meta or para methyl group in (10) or (11) are far away from the  $\text{--S}^-$  thus does not result in significant steric interaction.
  2. THF is an **aprotic solvent** and solvates mainly the cation but not the anion. Methanol is a **protic solvent** that could solvate both cations and anions. So in the reaction, the  $\text{--S}^-$  anion from (12), in addition to the steric factor mentioned in (a) is further solvated by the methanol molecules, further decreasing its nucleophilicity. So the yield of the product will be further reduced.

## **19/20 Test**

6.



This molecule is symmetrical so H and BH<sub>2</sub> could be attached to either carbon of the C=C hence no regioselectivity is possible.



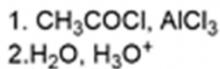
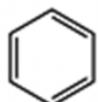
Steric factor will result in a 4-membered ring intermediate with the BH<sub>2</sub> attached to the less hindered carbon of the C=C. This is where regioselectivity is observed.

- a) Which of the following reagents will enable both compounds **F** and **G** to yield the same product? [For this question, consider only constitutional isomers. Ignore stereoisomers]
- BH<sub>3</sub> followed by H<sub>2</sub>O<sub>2</sub>, HO<sup>-</sup>
  - Hg(OAc)<sub>2</sub>/H<sub>2</sub>O followed by NaBH<sub>4</sub>
  - O<sub>3</sub> followed by Zn/H<sub>3</sub>O<sup>+</sup>
- b) For the selected reagents in Part (a), which of the compounds **F** and **G** will exhibit regioselectivity in the reaction? Explain.

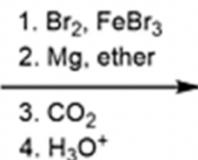
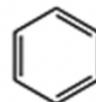
## 20/21 Final

Which of the following routes can be used to prepare benzoic acid?

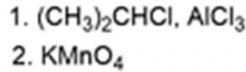
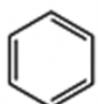
(I)



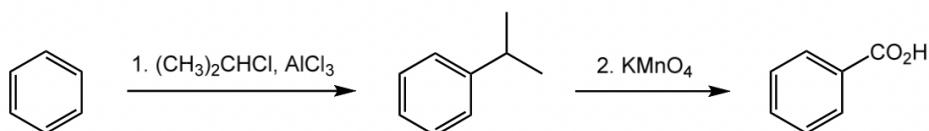
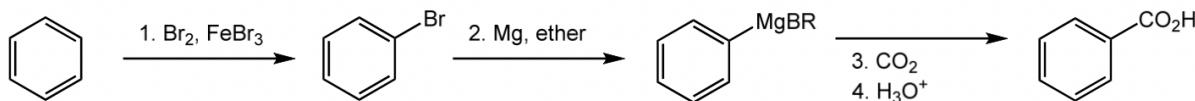
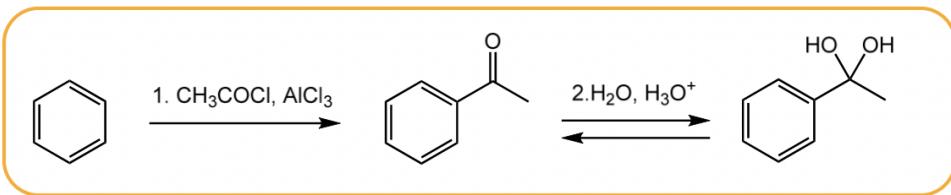
(II)



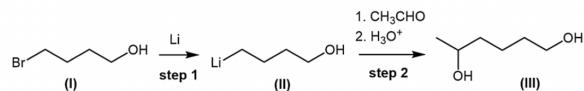
(III)



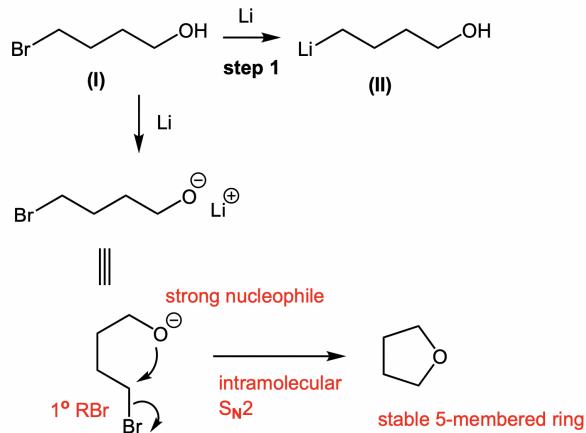
- (A) (I) and (II)  
**(B)** (II) and (III)  
(C) (I) and (III)  
(D) None of the routes  
(E) All of the routes



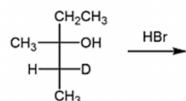
An attempt to prepare compound (III) from compound (I) via an organolithium reagent (II) failed. What is wrong with the following synthetic scheme? [Reminder: an organolithium reagent is similar to a Grignard reagent.]



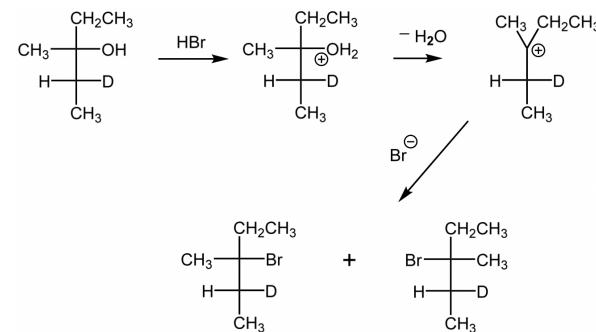
- (A) Lithium will promote an alternative reduction in step 1.
- (B) The aldehyde will only react with the hydroxyl group in step 2.
- (C)** An alternative substitution will occur in step 1.
- (D) A alternative dehydration will occur in step 2.



The following two reactants undergo a substitution reaction. The product (or product mixture) shows optical activity. Which of the following is true?

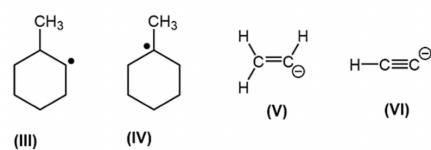
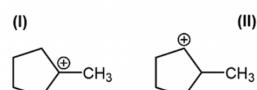


- (A) Only one chiral product is obtained
- (B)** A mixture of two diastereomers is obtained
- (C) A mixture of two enantiomers is obtained in uneven quantities
- (D) A mixture of two diastereomers is obtained. One is chiral and another is a meso compound

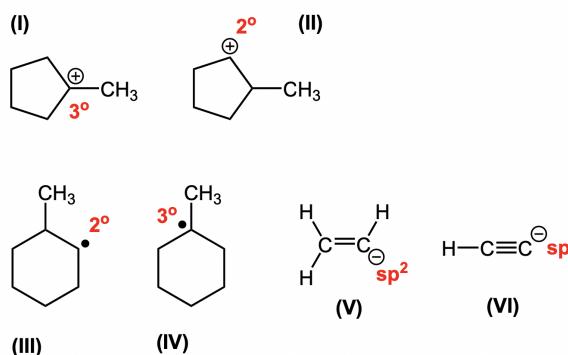


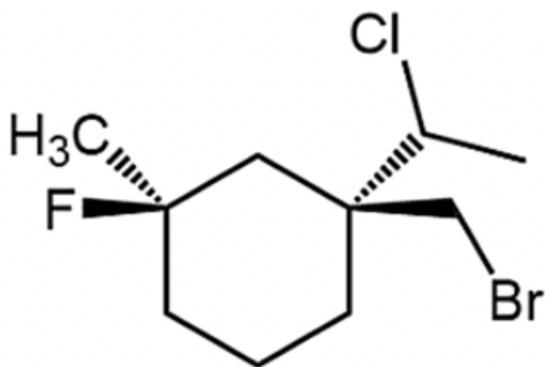
A pair of diastereomers;  
each is optically active

Carboradials, carbocations and carbanions are all reactive species. Which of the following sets contains the least stable species?

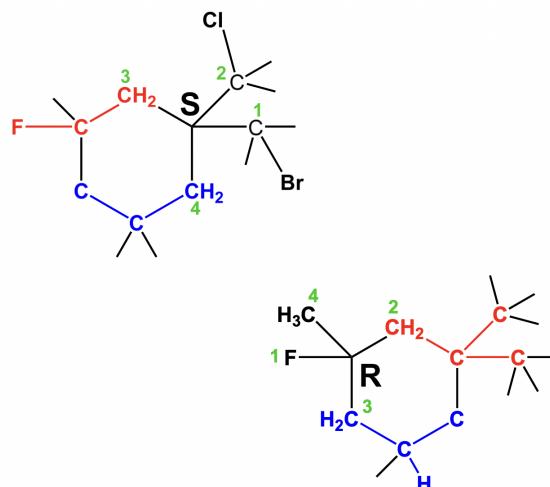


- (A) (I), (III) and (V)
- (B)** (II), (III) and (V)
- (C) (II), (IV) and (VI)
- (D) (I), (IV) and (V)
- (E) (II), (III) and (VI)
- (F) (I), (IV) and (VI)



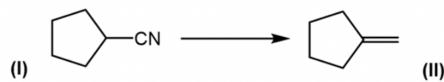


(1S, 3R)-1-bromomethyl-1-(1-chloroethyl)-3-fluoro-3-methylcyclohexane

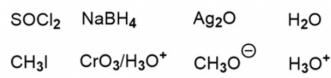


priority depends on the atom with the highest mass no.

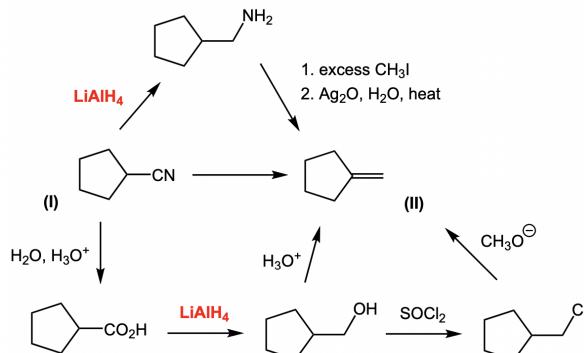
A synthesis of compound (II) from compound (I) is considered. Eight reagents as indicated are provided. How many synthetic routes could be designed?



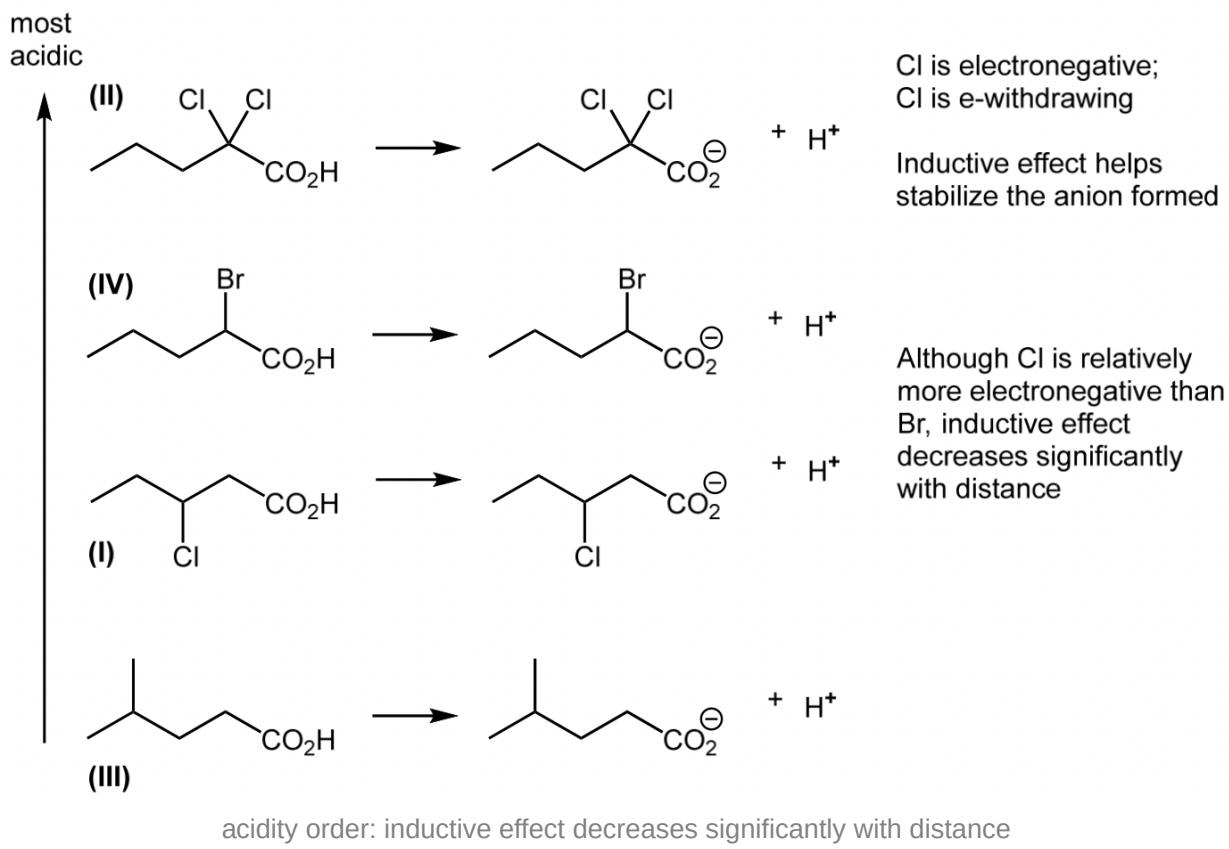
Eight reagents provided:



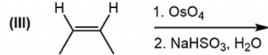
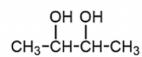
- (A) 3
- (B) 2
- (C) 1
- (D) No synthetic route could be designed.



- There may be up to three possible synthetic routes
- However, two reduction reactions are involved that will require the strong reducing agent:  $\text{LiAlH}_4$
- The  $\text{NaBH}_4$  provided cannot reduce a nitrile or a carboxylic acid.

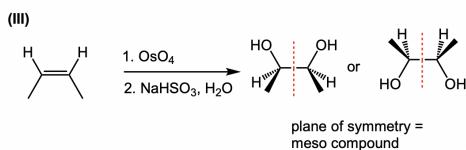
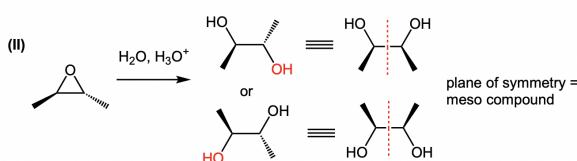
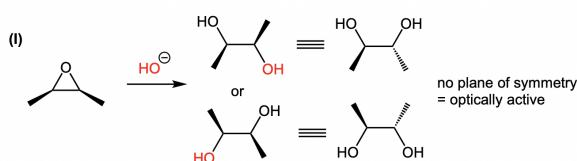


All the products formed in the following three reactions have the general formula:

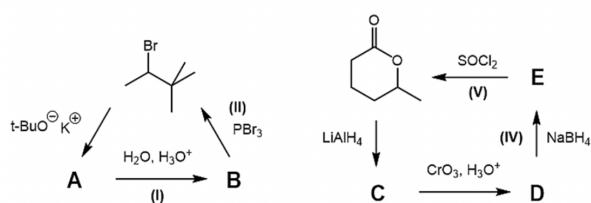


Which of the reactions will result in the formation of a meso compound?

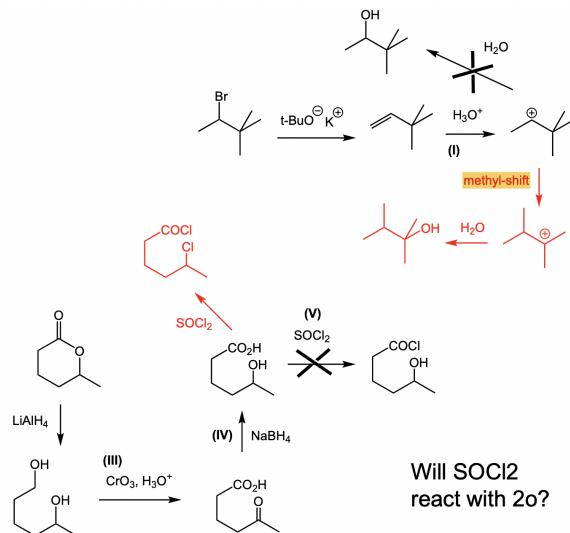
- (A) I & II
- (B) I & III
- (C)** II & III
- (D) I only
- (E) II only



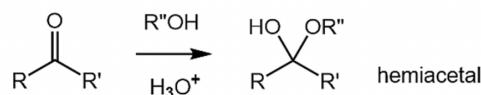
Which of the steps in the following two synthetic schemes will go wrong?



- (A) (I) and (III)
- (B) (I) and (IV)
- (C)** (I) and (V)
- (D) (II) and (III)
- (E) (II) and (IV)
- (F) (II) and (V)

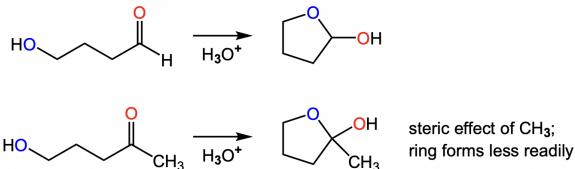
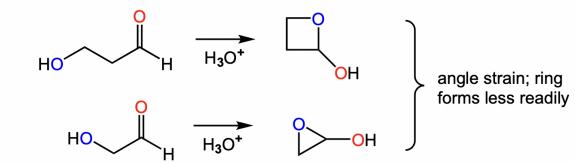


A hemiacetal could be prepared by the following reaction:



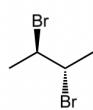
Which of the following most readily forms a cyclic hemiacetal under similar acid catalysis?

- (A) HO-CH2-CH2-C(=O)-H
- (B) HO-CH2-C(=O)-H
- (C)** HO-CH2-CH2-CH2-C(=O)-H
- (D) HO-CH2-CH2-CH2-C(=O)-CH3

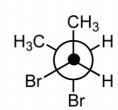


## 20/21 Quiz 1

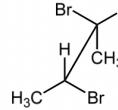
Which of the following projections represent the same stereoisomer:



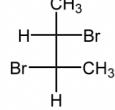
(I)



(II)

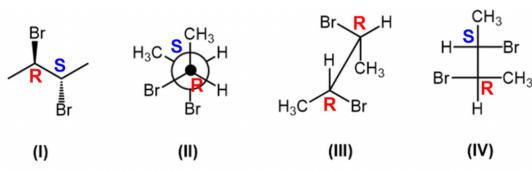


(III)



(IV)

- (A) (I) and (II)
- (B) (II) and (IV)
- (C) (I), (II) and (III)
- (D)** (I), (II) and (IV)
- (E) (II), (III) and (IV)



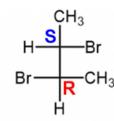
(I)



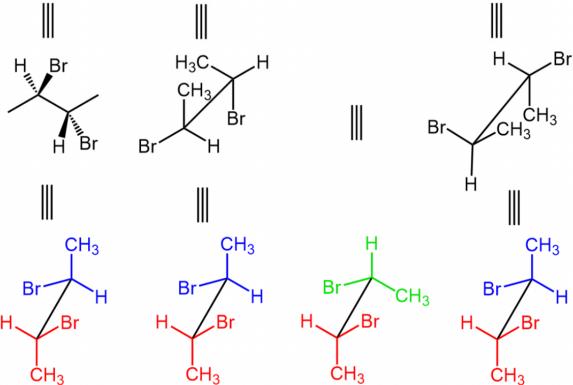
(II)



(III)

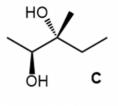
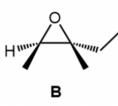
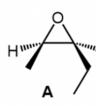


(IV)



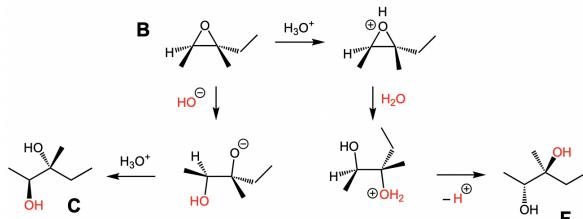
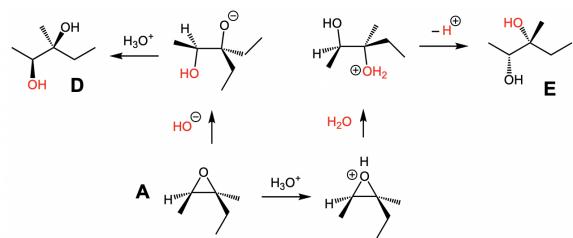
1. If you are able to assign R,S configuration directly to (I) to (IV), you could immediately see that (I), (II) and (IV) are (R,S) but (III) is (R,R).
2. Or you have to convert (I), (II), (III) and (IV) (retaining the correct stereochemistry) to a common projection, e.g. the Sawhorse as illustrated. Then (III) will be the only different stereochemistry.

You are given A and B as starting materials. Which combination will you use to prepare compound C?



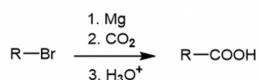
- (I) : 1. mCPBA, 2.  $\text{HO}^-$ , 3.  $\text{H}_3\text{O}^+$
- (II) : 1. mCPBA, 2.  $\text{H}_2\text{O}$ ,  $\text{H}_3\text{O}^+$

- (A) A and (I)
- (B)** B and (I)

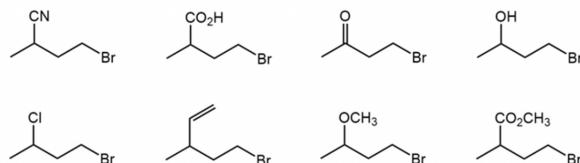


## 20/21 Quiz 2

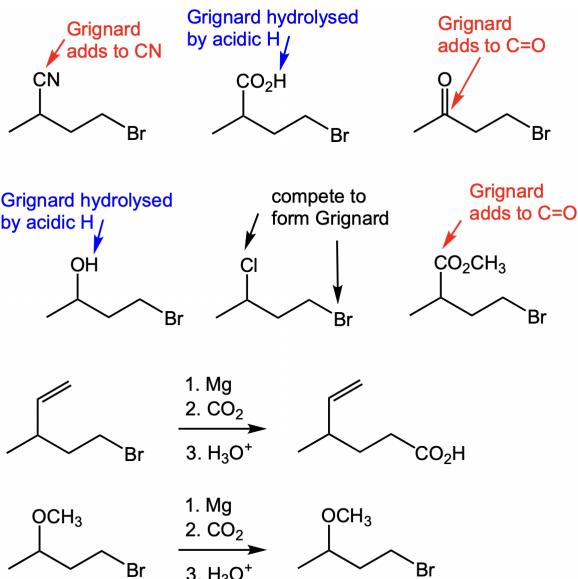
The following is a common synthesis for carboxylic acids.



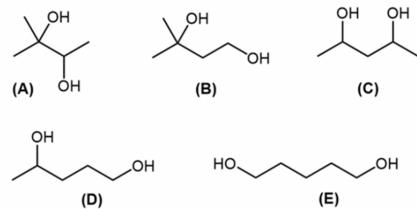
How many of the following compounds could be used in preparing the corresponding carboxylic acids by the above synthesis?



- (A) None of the compounds  
 (B) One  
 (C) Two



An unknown compound is believed to be one of the following compounds with a common molecular formula of  $\text{C}_5\text{H}_{12}\text{O}_2$ .



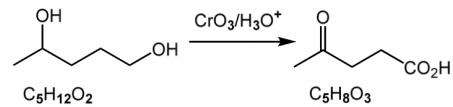
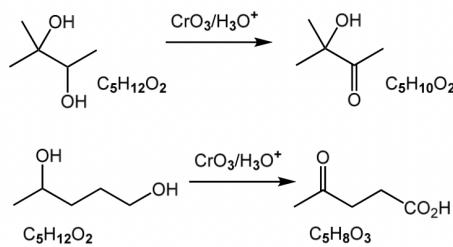
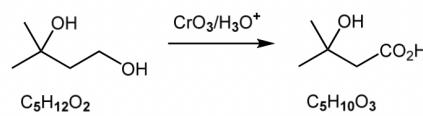
- a) When the unknown was treated with one equivalent of  $\text{CH}_3\text{COCl}$ , a major product with a molecular formula of  $\text{C}_7\text{H}_{14}\text{O}_3$  could be isolated in 90% yield.  
 b) When the unknown was oxidized with  $\text{CrO}_3/\text{H}_3\text{O}^+$ , a product with a molecular formula of  $\text{C}_5\text{H}_{10}\text{O}_3$  was isolated.

The identity of the unknown is likely to be:

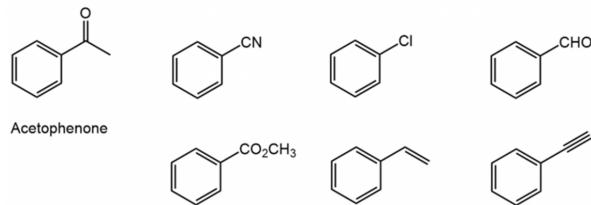
- (A)  
 (B)

a) All compounds are  $\text{C}_5\text{H}_{12}\text{O}_2$ -diols. When one equivalent of  $\text{CH}_3\text{COCl}$  is used, only one OH reacts to form a  $\text{C}_7$ -compound. So the two OH groups should be different to offer CHEMOSELECTIVITY  
 --- this rules out (C) and (E).

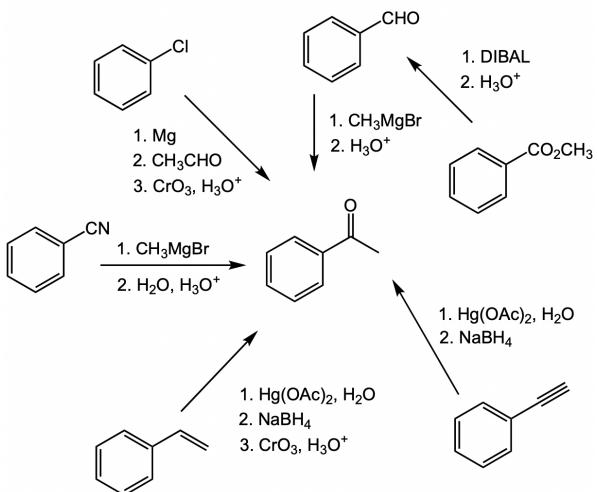
b)  $\text{CrO}_3/\text{H}_3\text{O}^+$  is an oxidation condition. Only  $1^\circ$  or  $2^\circ$  alcohols could be oxidised.  $3^\circ$  alcohols should remain intact.  
 --- oxidation still applies to remaining (A) [has one  $2^\circ$  OH], (B) [has one  $1^\circ$  OH] and (D) [has one  $1^\circ$  and one  $2^\circ$  OH].  
 BUT after oxidation, the molecular formula of the product is  $\text{C}_5\text{H}_{10}\text{O}_3$ , two H less and one O more than the starting diol.  
 --- this is only consistent with (B):



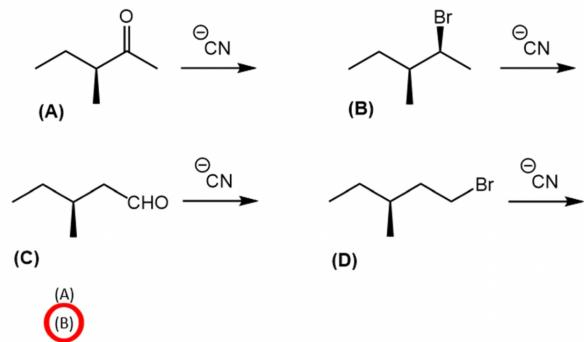
How many of the following compounds could be used to prepare acetophenone? You may use any organic or inorganic reagents. You may use any number of reaction steps in your synthesis.



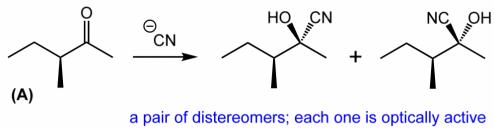
- (A) All of the compounds  
(B) Five  
(C) Four  
(D) Three  
(E) Two



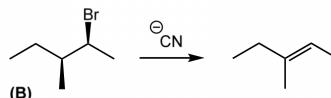
The following reactions are carried out separately. Which product or product mixture is most likely to show no optical activity?



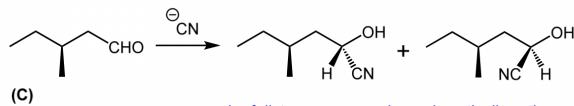
- (A)  
(B)



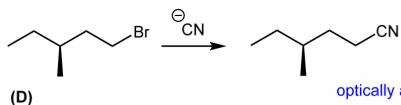
a pair of diastereomers; each one is optically active



(a) 2° RBr; (b) steric hindered; (c) S<sub>N</sub>2 suppressed. (d) E2 occurs.  
 (e) alkene formed is achiral - shows no optical activity.



a pair of diastereomers; each one is optically active



optically active compound

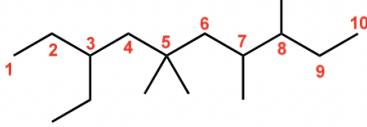
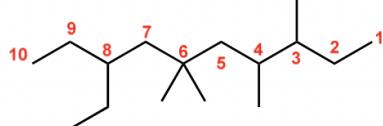
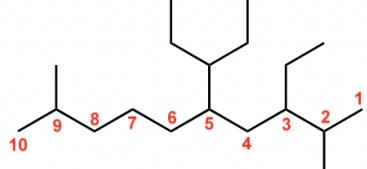
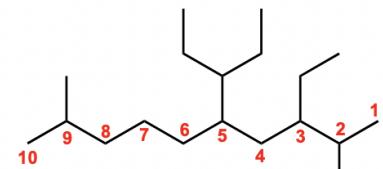
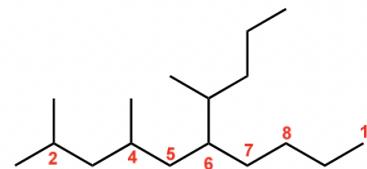
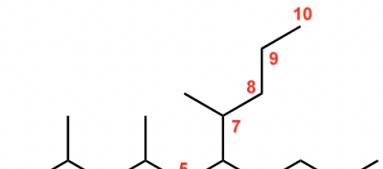
# 21/22 Test 1

Which of the following are incorrect IUPAC names?

- (I) 3-Ethyl-5,5,7,8-tetramethyldecane
- (II) 3-Ethyl-2,9-dimethyl-5-(1-ethylpropyl)decane
- (III) 2,4-Dimethyl-6-(1-methylbutyl)decane

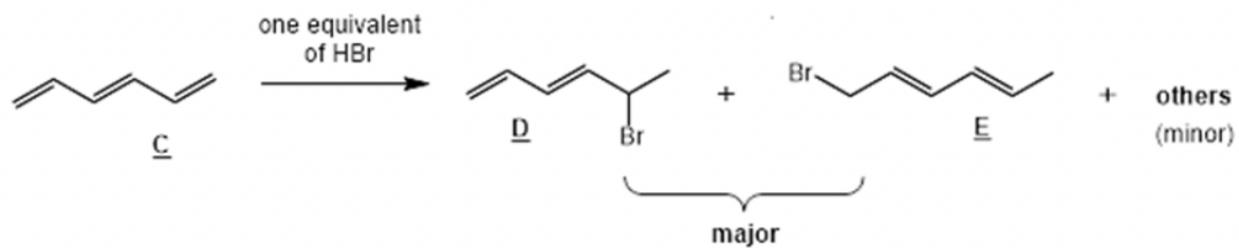
(9 Marks)

- (A) (I) and (II)
- (B) (I) and (III)
- (C) (II) and (III)
- (D) (I), (II) and (III)**
- (E) All three IUPAC names are in fact correct

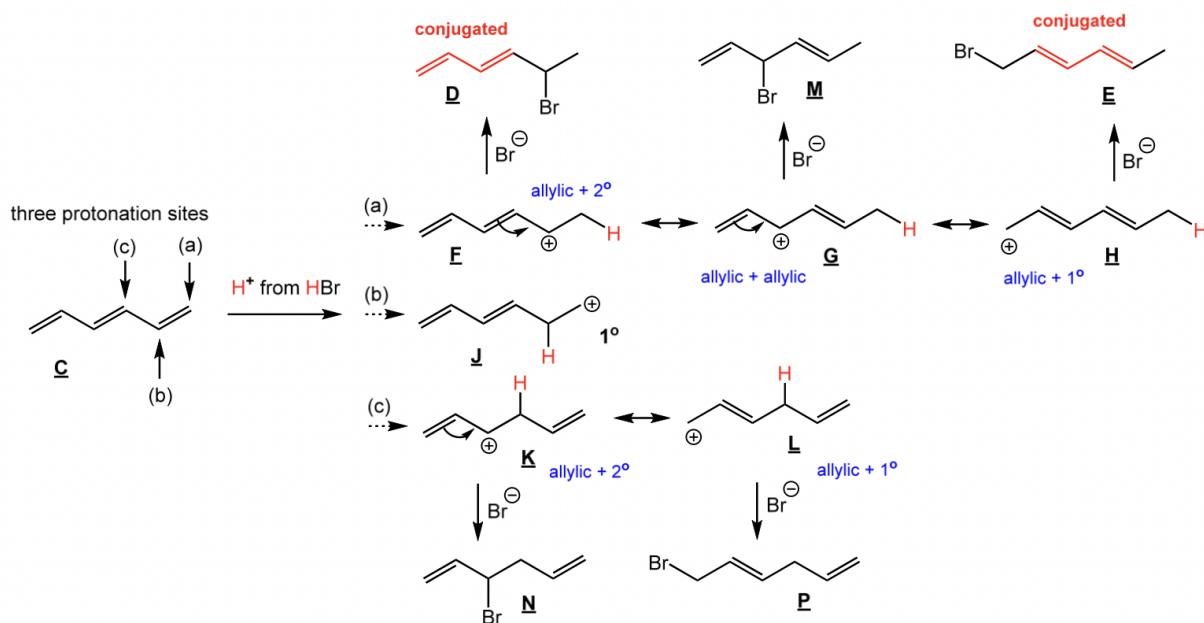
Incorrect	Reason	Correct
3-Ethyl-5,5,7,8-tetramethyldecane 	<ol style="list-style-type: none"> <li>Numbering from end with lowest number for first substituent – both ends have substituent at 3<sup>rd</sup> carbon</li> <li>Numbering from end with lowest number for second substituent – from right end, methyl at 4<sup>th</sup> carbon; from left end, methyl at 5<sup>th</sup> carbon</li> </ol>	 8-Ethyl-3,4,6,6-tetramethyldecane
3-Ethyl-2,9-dimethyl-5-(1-ethylpropyl)decane 	<ol style="list-style-type: none"> <li>“di” in “dimethyl” is not included in alphabetical order consideration</li> <li>“ethylpropyl” is a complete name as “e” in alphabetical order</li> </ol>	 3-Ethyl-5-(1-ethylpropyl)-2,9-dimethyldecane
2,4-dimethyl-6-(1-methylbutyl)decane 	<ol style="list-style-type: none"> <li>Parent should have most substituents</li> <li>Incorrect name only has three substituents</li> <li>Correct name has four substituents</li> </ol>	 6-butyl-2,4,7-trimethyldecane

10. 1,3,5-Hexatriene C is treated with one equivalent of HBr.

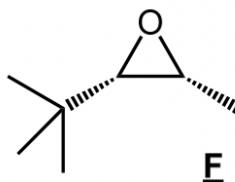
Among a number of possible products formed, compounds D and E are isolated as major products. Give an explanation to this observation.

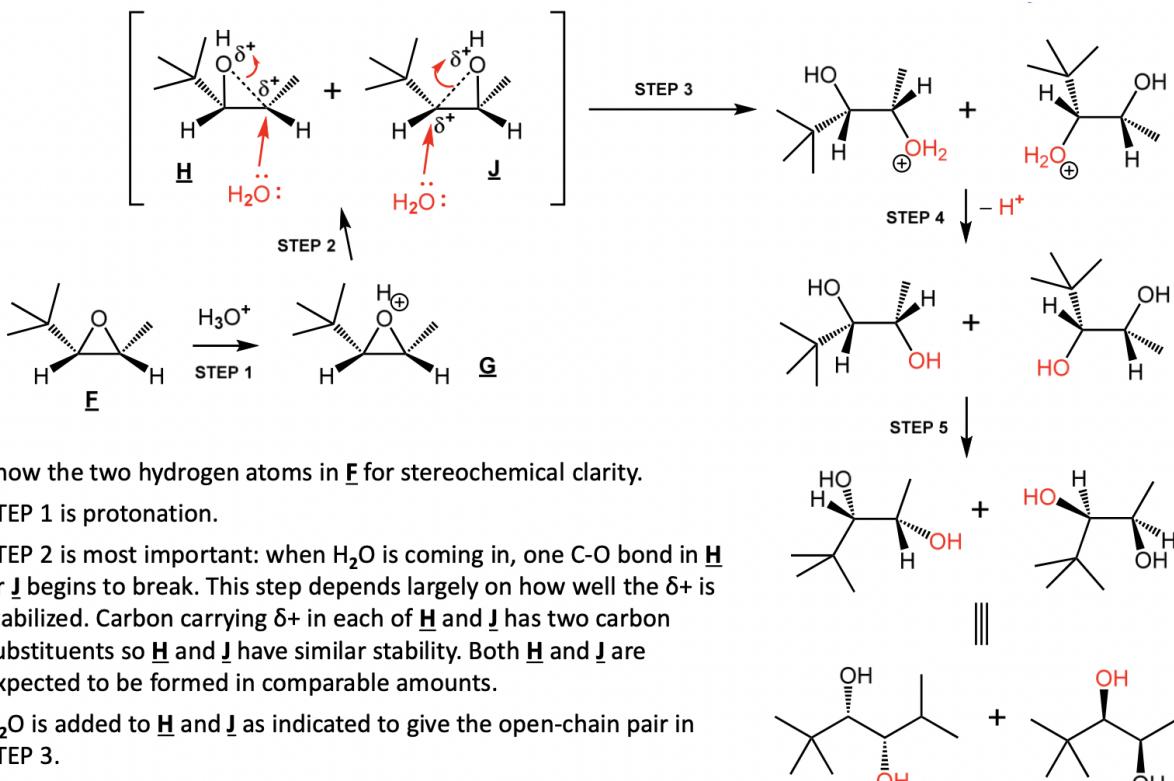


- a) Consider **STEP 1**: the protonation of triene to form a carbocation. There are 3 possible sites to be protonated. **The more stable the carbocation, the faster/easier it is formed.**
- Carbocation from path (b) gives a highly unstable primary carbocation **J**, so path (b) is very minor.
  - Both paths (a) & (c) give allylic + 2° carbocations **F** and **K** respectively, so both these paths are preferred.
- b) **STEP 2**: carbocation reacts with  $\text{Br}^-$  to form a product. **The more stable the product, the faster the reaction.**
- F** is in resonance with **G** and **H**; **K** is in resonance with **L**. In principle, products derived from properties of these resonance structures could be formed.
  - D** and **E** are **conjugated dienes**, so they are relatively more stable due to conjugation effect – they are formed faster/easier as **major products**.
  - M**, **N** & **P** are isolated dienes, so they are relatively less stable than D and E.



Provide the mechanism and products for the aqueous acid-catalyzed epoxide opening reaction of compound **E**, including appropriate stereochemistry.

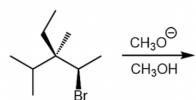




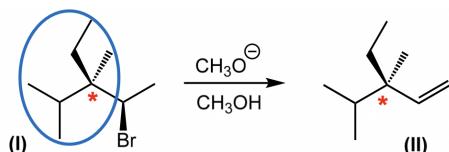
- a) Show the two hydrogen atoms in E for stereochemical clarity.
- b) STEP 1 is protonation.
- c) STEP 2 is most important: when  $\text{H}_2\text{O}$  is coming in, one C-O bond in H or J begins to break. This step depends largely on how well the  $\delta^+$  is stabilized. Carbon carrying  $\delta^+$  in each of H and J has two carbon substituents so H and J have similar stability. Both H and J are expected to be formed in comparable amounts.
- d)  $\text{H}_2\text{O}$  is added to H and J as indicated to give the open-chain pair in STEP 3.
- e) STEP 4 is deprotonation.
- f) STEP 5 involves rotation about central C-C bond to give the pair with the parent skeleton in the screen or slide plane.
- g) Hiding the H atoms (for simplicity) will give the line structures of the two products K and L, respectively.

## 21/22 Test 2

In the following reaction, the product (or product mixture) shows optical activity. Which of the following is true?

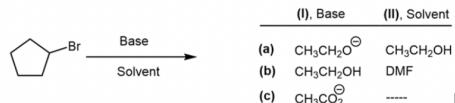


- (A) Only one chiral product is obtained  
 (B) A mixture of two diastereomers is obtained  
 (C) A mixture of two enantiomers is obtained in uneven quantities  
 (D) A mixture of two diastereomers is obtained. One is chiral and another is a meso compound



1. Substrate (I) is a 2° alkyl bromide that could go through any of E1, E2,  $S_N1$  or  $S_N2$ .
2.  $\text{CH}_3\text{O}^-$  is a strong base and a strong nucleophile that favors E2 or  $S_N2$ .
3. The alkyl group circled blue in substrate (I) is sterically bulky in discouraging  $S_N2$ .
4. The reaction undergoes an E2 mechanism to form compound (II).
5. The chiral centre (\*) is retained going from (I) to (II).
6. Compound (II) is the only product formed that is optically active.

Select the best combination for an E1 reaction using the following substrate:



- (A) (I)(a) and (II)(a)  
 (B) (I)(b) and (II)(a)  
 (C) (I)(c) and (II)(a)  
 (D) (I)(a) and (II)(b)  
 (E) (I)(c) and (II)(b)

- An E1 reaction involves the formation of carbocation as the rate determining step. Any factor that stabilizes the carbocation formation will enhance E1 reaction.

- E1 is independent of the base used.

