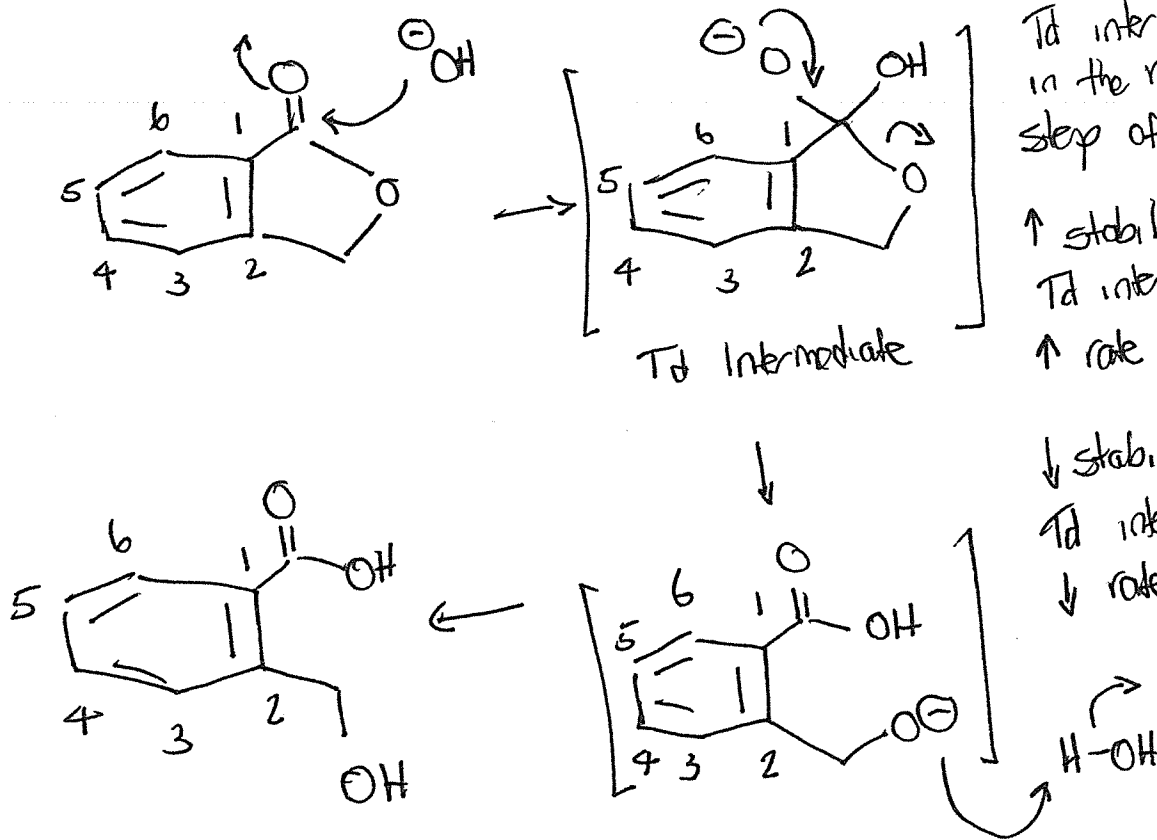


1. Base-Catalyzed Hydrolysis of benzoate esters



Td intermediate forms in the rate-determining step of the rxn.

↑ stability of the Td intermediate  
 ↑ rate

↓ stability of the Td intermediate,  
 ↓ rate

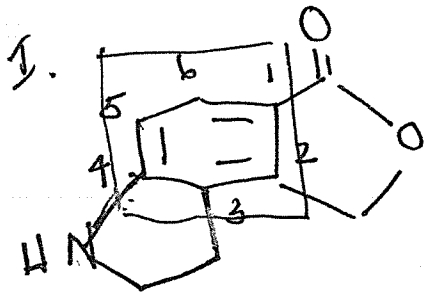
Td intermediate is STABILIZED when ring is ⊕ via substituent effects (determined with  $\sigma$  values)

⊕ RING ↑ RATE FASTER

Td intermediate is DESTABILIZED when ring is ⊖

⊖ RING ↓ RATE SLOWER

So most ⊕, or least ⊖ ring will react FASTEST

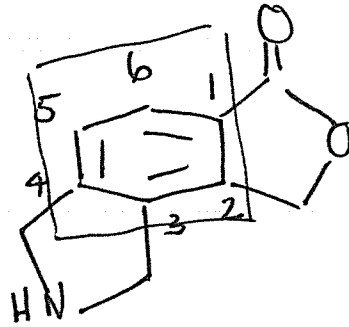


$C_3$   $CH_3$   $\sigma_m = -0.07$

$C_4$  AMINO  $\sigma_p = -0.66$

$\boxed{-0.73}$

II.

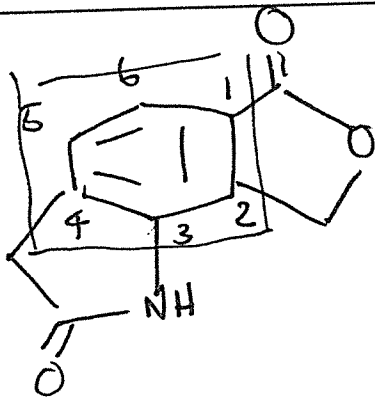


$C_3$   $CH_3$   $\sigma_m = -0.07$

$C_4$   $CH_3$   $\sigma_p = -0.17$

$\boxed{-0.24}$

III.

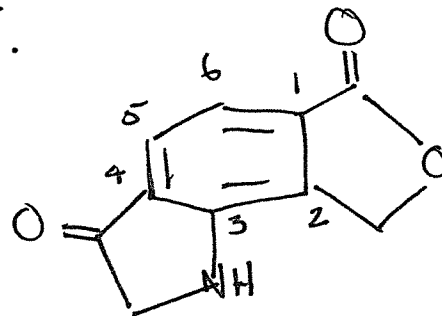


$C_3$  ACETAMIDO  $\sigma_m = +0.21$

$C_4$   $CH_3$   $\sigma_p = -0.17$

$\boxed{+0.04}$

IV.



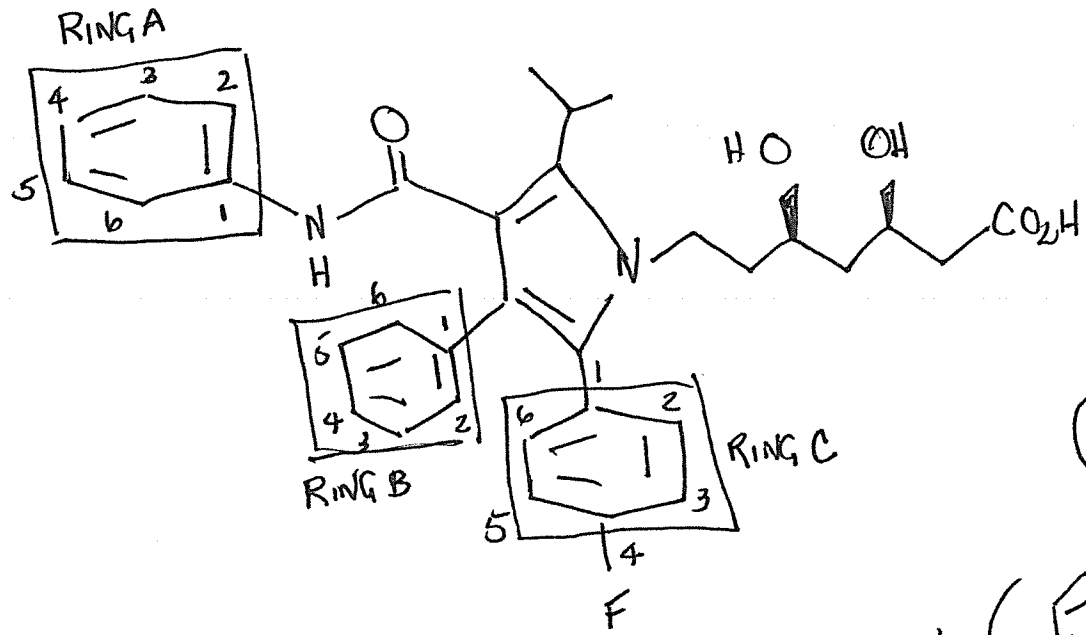
$C_3$  AMINO  $\sigma_m = -0.16$

$C_4$  ACETY  $\sigma_p = +0.5$

$\boxed{+0.34}$


$IV > III > II > I$  (E)

2.



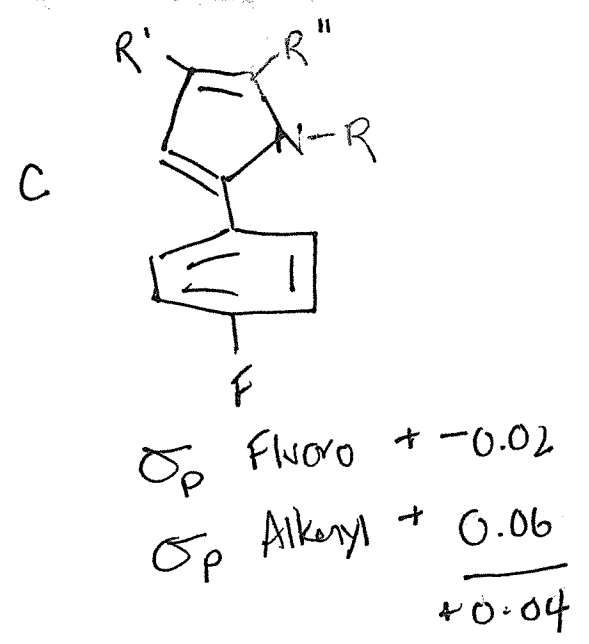
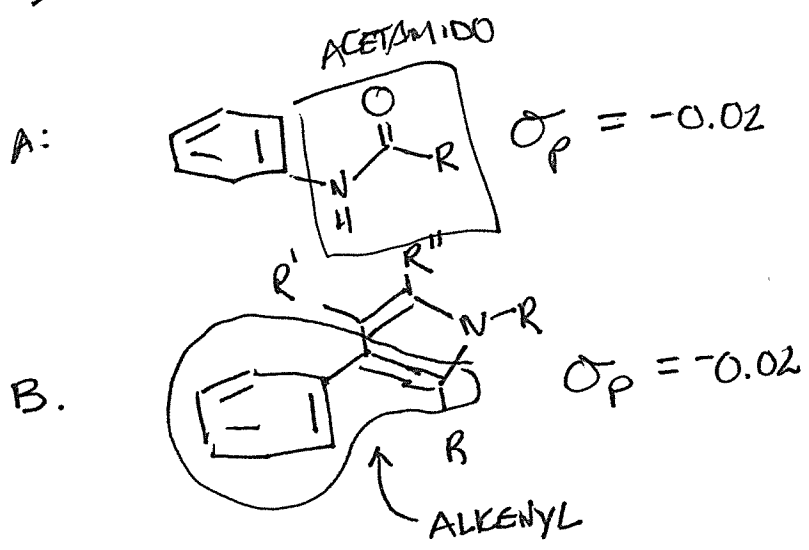
- I. TRUE
- II. FALSE
- III. FALSE
- IV. FALSE

(A)

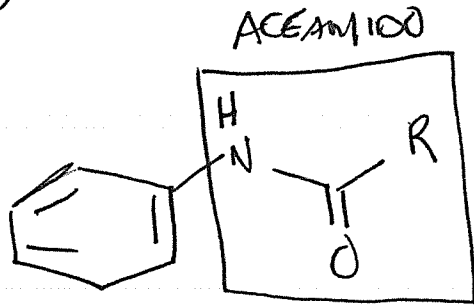
I. Ring C is PARA substituted. The F- and pyrole (  ) have a 1,4 - relationship on this DISUBSTITUTED benzene ring.

II. The F is a DEACTIVATOR (HALOGEN EWG by INDUCTION)  
 The substituent at C<sub>1</sub> is C atom part of alkene (i.e. EXTERNAL π bond, EWG by RESONANCE)  
 EWG "pull" electrons out of the ring and make ring more ⊕ and LESS reactive DEACTIVATORS

III. The most ACTIVATED rings are A and B b/c MOST ⊖

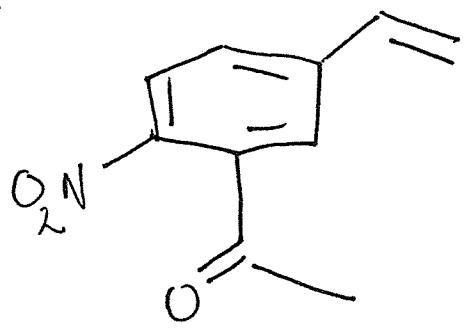


IV.



The substituent on ring A is an AMIDE and is NOT an ionizable functional group (i.e. NOT AN ACID) NOT A BASE

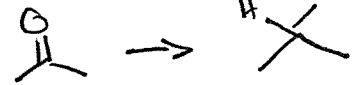
3.



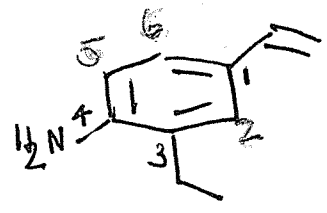
2-NITRO-5-VINYL ACETOPHENONE

I. Zn(Hg), HCl  
CLEMMENSEN

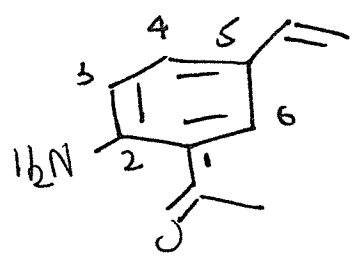
Reduces BOTH



NOT ALKENES

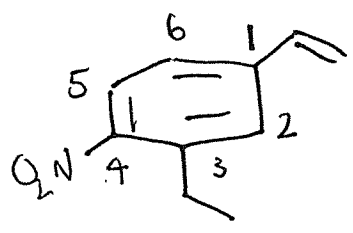
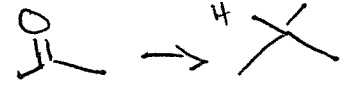


II. SnCl<sub>2</sub>, HCl  
Reduces ONLY  
 $NO_2 \rightarrow NH_2$



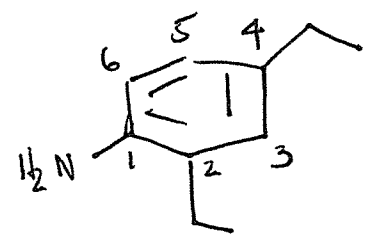
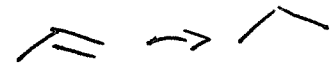
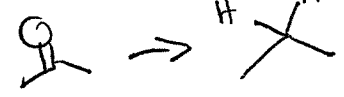
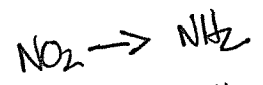
2-AMINO-5-VINYL ACETOPHENONE

III. H<sub>2</sub>NNH<sub>2</sub>, KOH  
WOLFF-KISHNER  
Reduces only



3-ETHYL-4-NITRO STYRENE

IV. H<sub>2</sub>, Pt  
CATALYTIC HYDROGENATION  
Reduces all



2,4-DIETHYLANILINE

(C)

4. Reaction of an alcohol with  $H_3PO_4$  is an  $E_1$  elimination

The mechanism involves formation of a carbocation in the rate determining step of the reaction. The most STABLE carbocation forms the fastest. Carbocation stability is determined by the following factors: SUBSTITUTION:  $3^\circ > 2^\circ > 1^\circ$

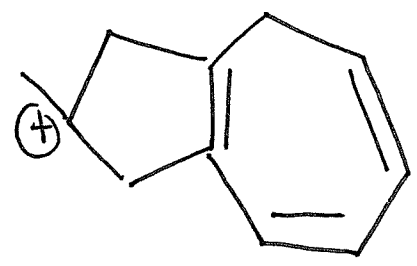
For allylic carbocations, the more resonance forms associated w/ the carbocation, the more stable the carbocation

RESONANCE: Allylic  $>$  Alkyl

AROMATIC: Aromatic  $>$  Allylic  $>$  Alkyl

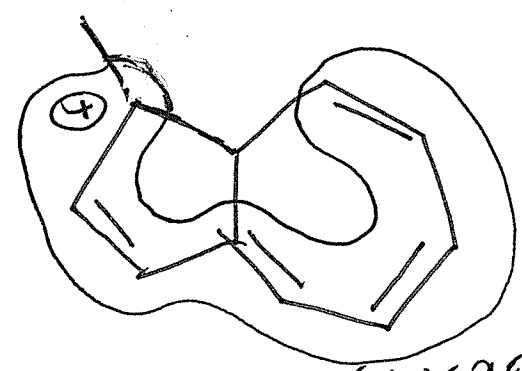
IV  $>$  II  $>$  III  $>$  I (D)

I.



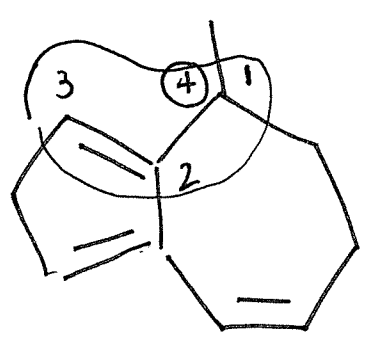
3° ALKYL CARBOCATION

II.



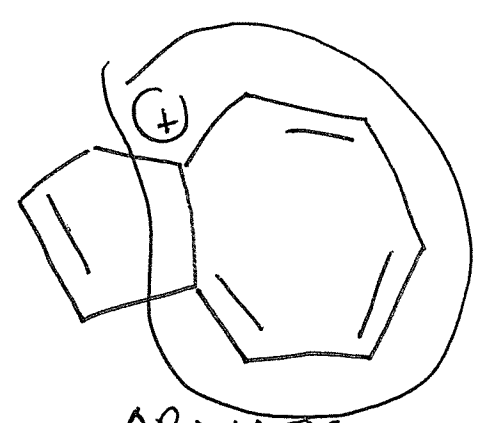
3° ALLYLIC (MULTIPLE RESONANCE FORMS)

III.



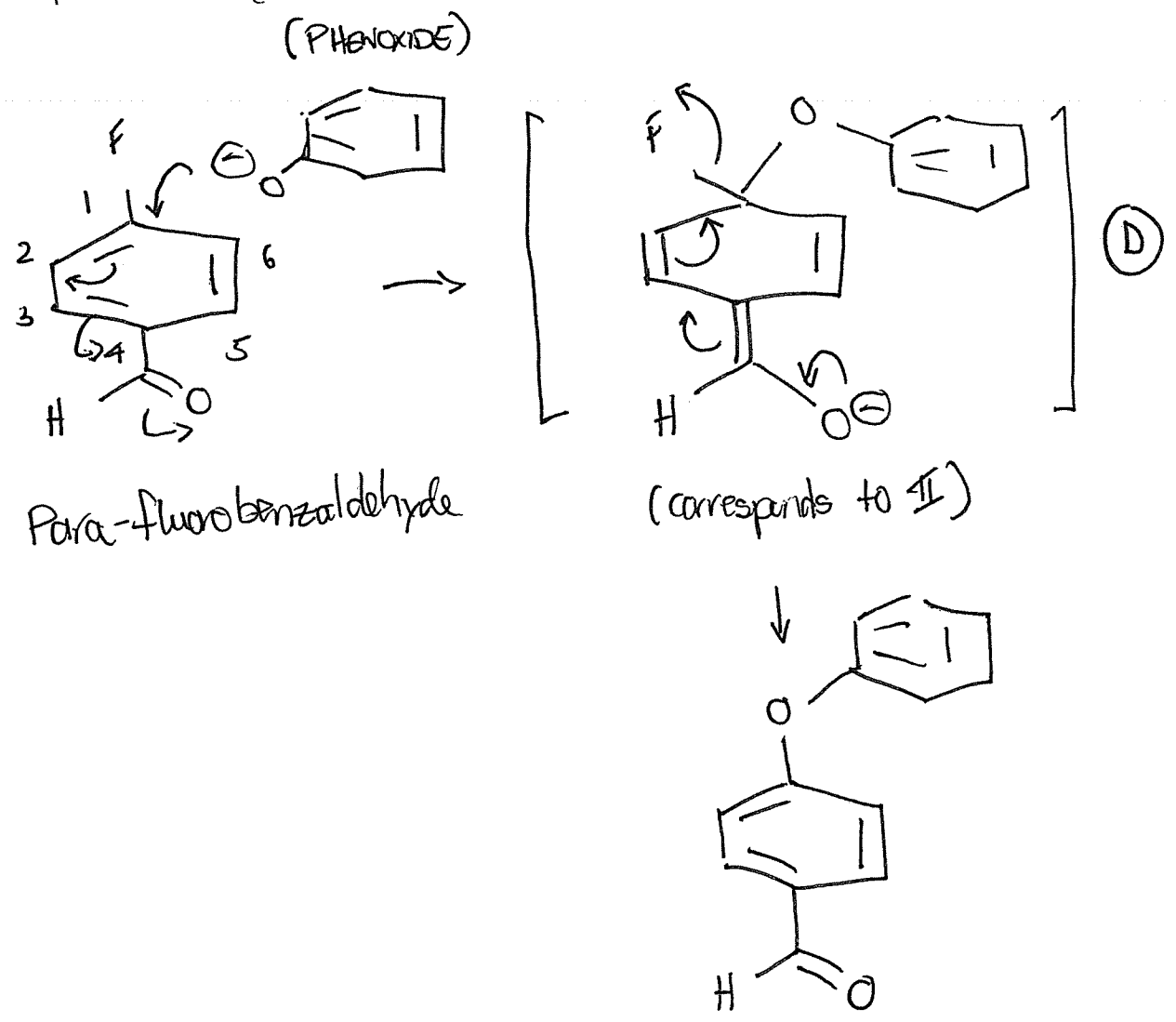
3° ALLYLIC CARBOCATION (ONE ADDITIONAL RESONANCE FORM)

IV.

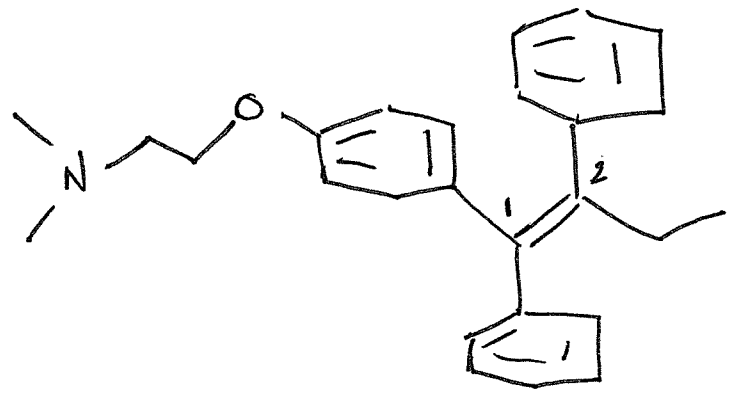


AROMATIC

5. Reaction of para-fluorobenzaldehyde with phenoxide is a nucleophilic aromatic substitution reaction.



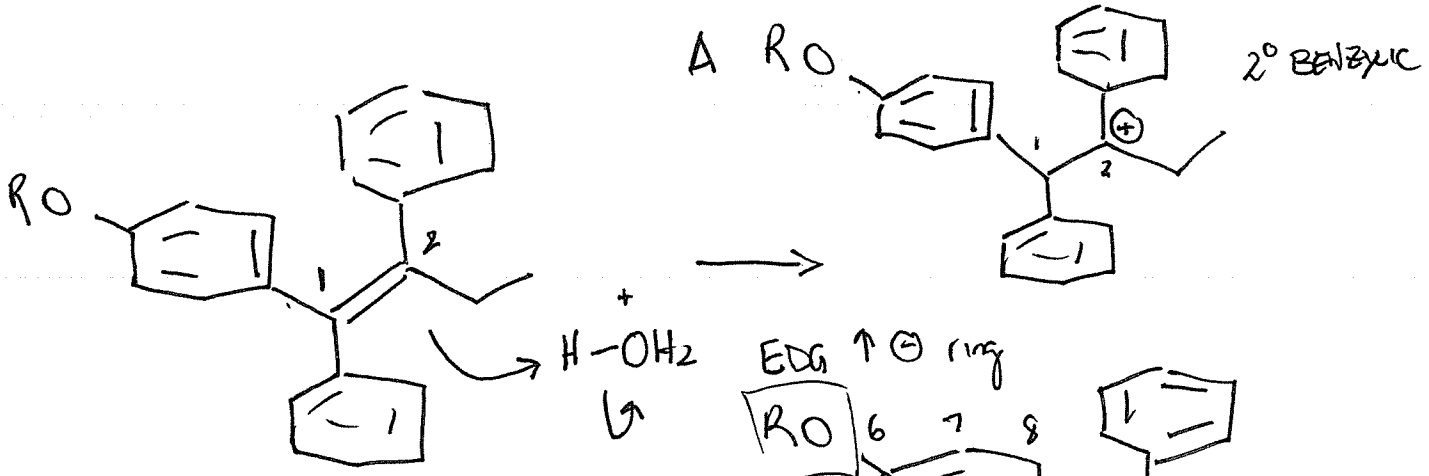
6. Reaction of tamoxifen with  $H_3O^+$  is an electrophilic addition of a STYRENE.



The C<sub>1</sub>-C<sub>2</sub> carbons represent the alkenyl group of the styrene.

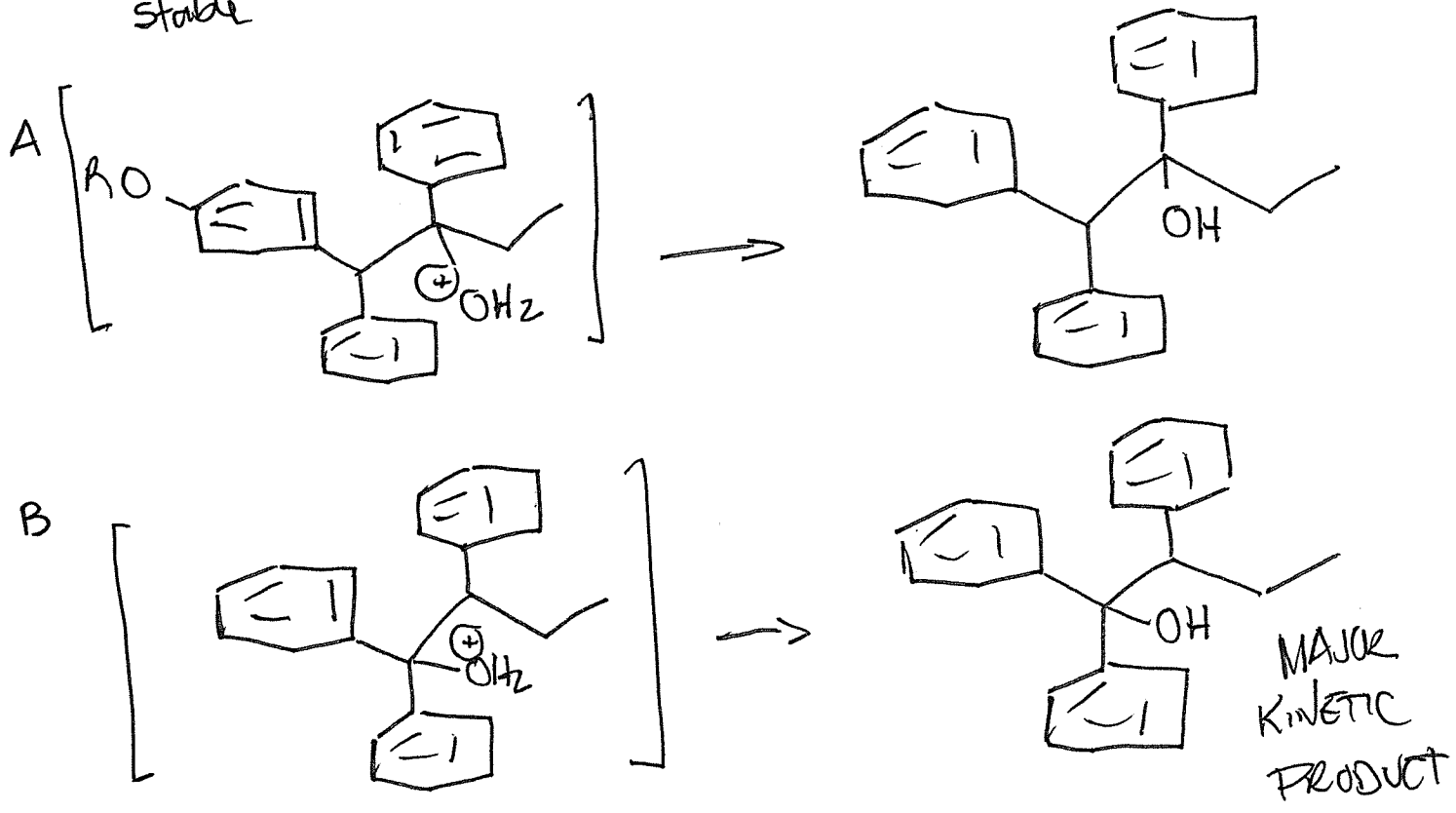
The rxn energy diagram is derived from the mechanism of the rxn.

6. (CONT'D)

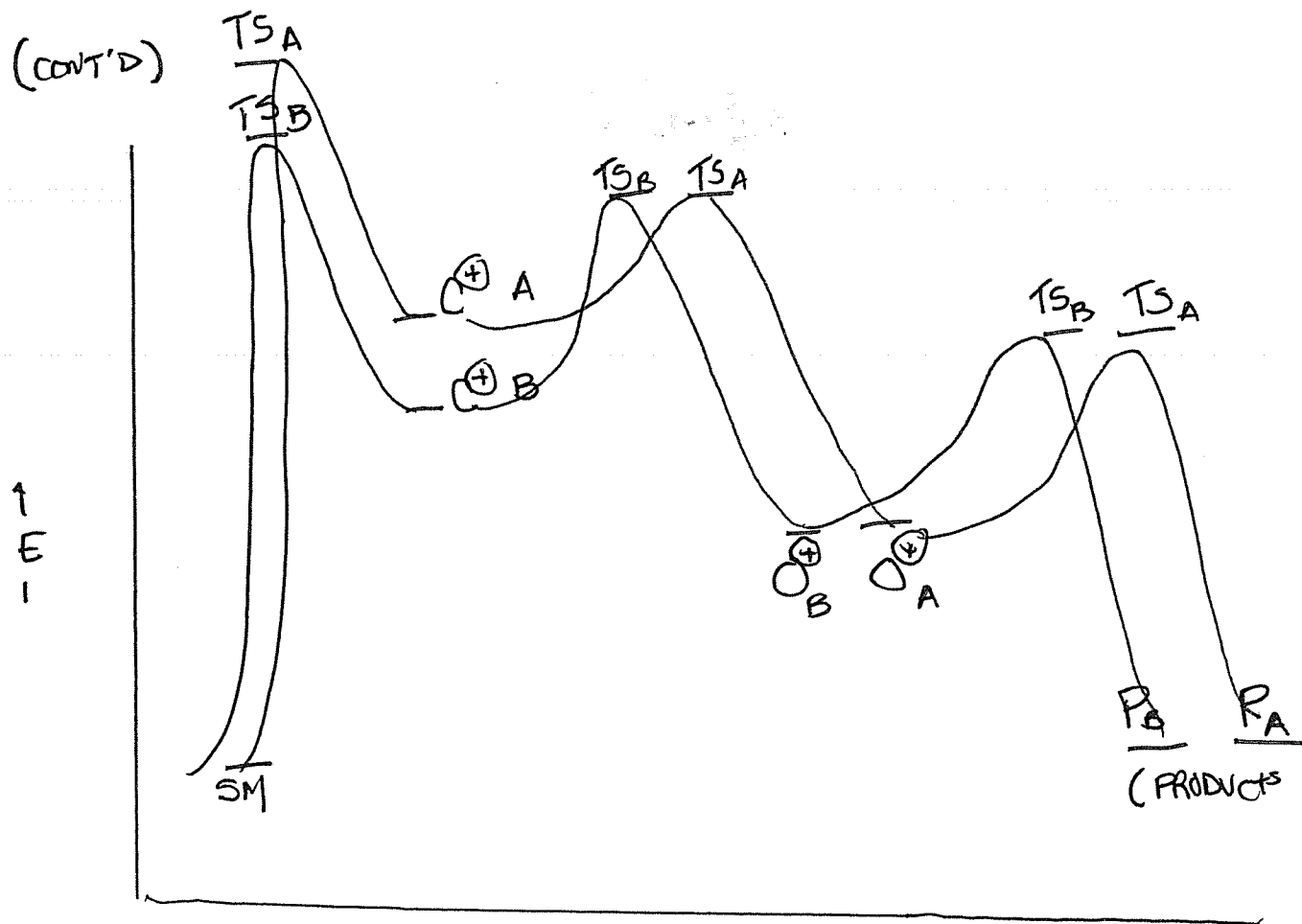


The  $\pi$  e $^-$  of the alkene react w/  $H^+$  to form two carbocations. @ C<sub>1</sub> and C<sub>2</sub>. C<sub>1</sub> carbocation (B) is more stable.

Each of the two carbocations continues to react w/ H<sub>2</sub>O to form two oxonium ion intermediates. Both are equally stable.



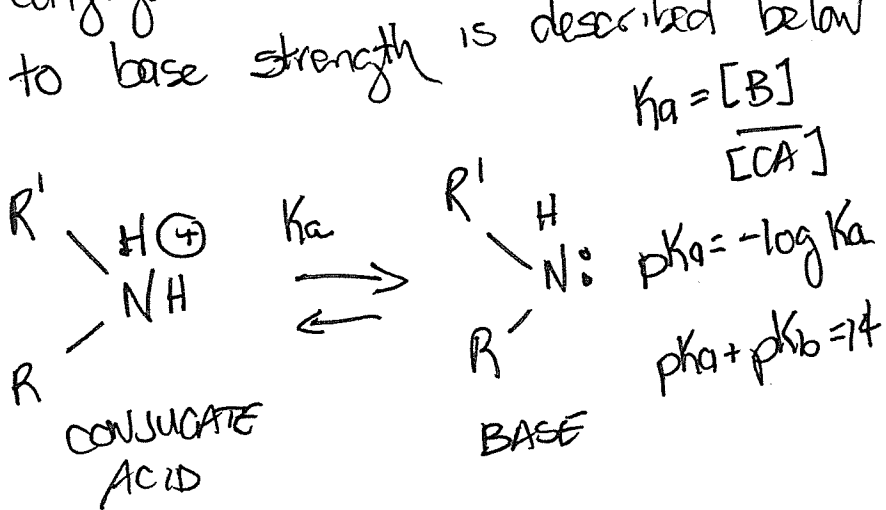
6. (CONT'D)



This diagram corresponds to choice d.

(D)

7. Tetraoic contains five nitrogen atoms, each of which can behave as a base by accepting a proton ( $H^+$ ) to form a conjugate acid. The strength of the base (i.e. how readily it accepts a proton) is represented by the  $pK_a$  of its conjugate acid. The relationship of the conjugate acid  $pK_a$  to base strength is described below

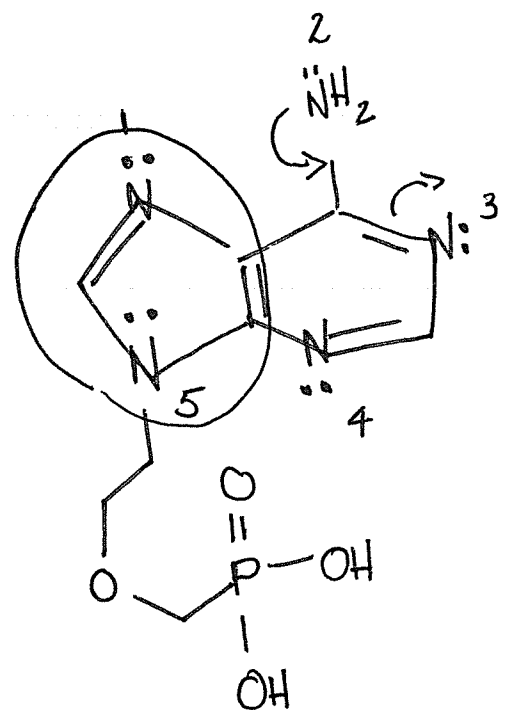


$\uparrow$  stability of [B]  
 $\uparrow$  concentration of [B]  
 $\uparrow K_a, \downarrow pK_a, \uparrow pK_b$   
 If B is very stable, specifically if stability dependent on lone pair  $pK_b$  is high,  $pK_a$  low



# 7. (CONT'D)

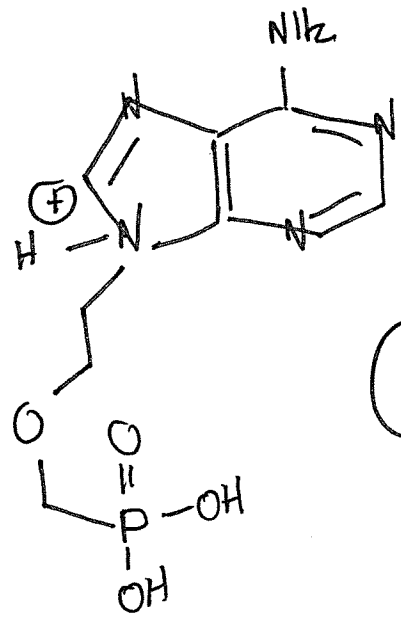
If the lone pair on N is part of aromatic system, BASE IS VERY stable and will have VERY LOW pKa and HIGH pKb  
 WEAK BASE



Each N is labeled as 1, 2, 3, 4 or 5  
 The lone pairs on N<sub>1</sub>, N<sub>3</sub> and N<sub>4</sub> are NOT involved in resonance or required as part of an aromatic ring, so these lone pairs are very available to react w/H<sup>+</sup> (STRONG BASES)

The N<sub>2</sub> nitrogen lone pair is involved in resonance so it is less available to accept a proton compared to N<sub>1</sub>, N<sub>3</sub> and N<sub>4</sub>.

The lone pair on N<sub>5</sub> is part of the AROMATIC SYSTEM in the circled part of the structure at the top right. The conjugate acid that is generated from this N<sub>5</sub> will have the LOWEST pKa and highest pKb

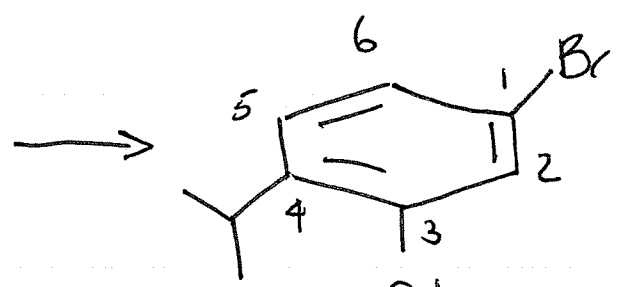


(A)

8.

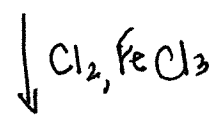
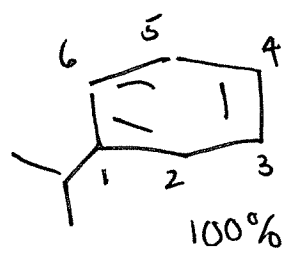
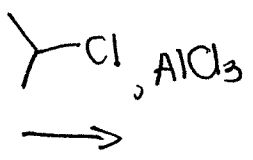
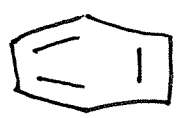


BENZENE



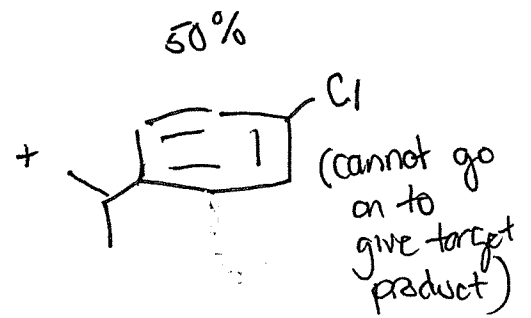
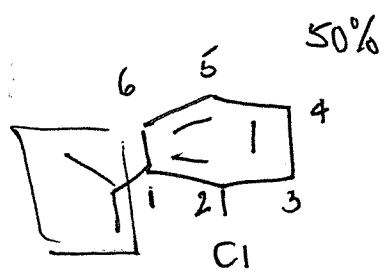
1-BROMO-3-CHLORO-ISOPROPYL BENZENE

1.

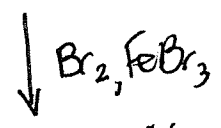


ISOPROPYL @ C1  
IS AN ACTIVATOR  
and o,p-director  
DIRECTS TO C2 (or C6)  
and C4

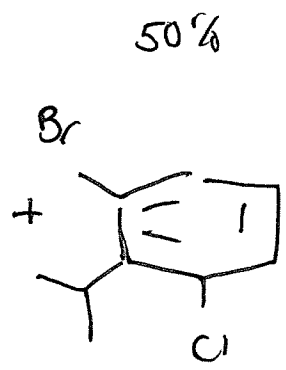
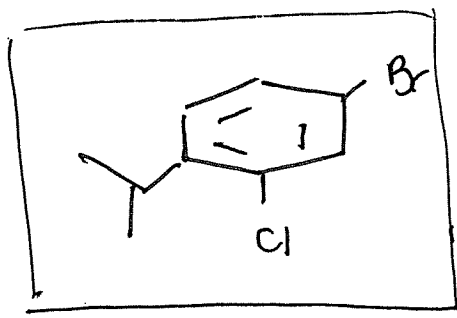
ISOPROPYL @ C1  
ACTIVATOR, ortho, para DIRECTOR  
DIRECTS TO C4, C6



Cl @ C2  
DEACTIVATOR  
DIRECTS TO C3, C5



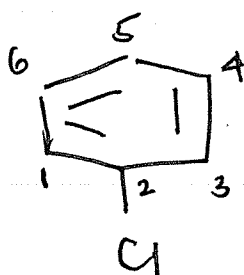
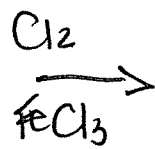
Rxn FOLLOWS ACTIVATOR  
NOT DEACTIVATOR



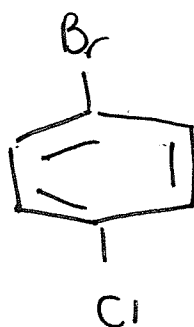
This product represents 25% of theoretical yield overall.

TARGET PRODUCT

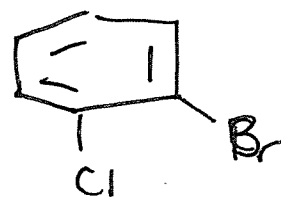
I.



Cl @ C<sub>2</sub> is a DEACTIVATOR,  
O,P-DIRECTOR  
DIRECTS TO C<sub>3</sub>, C<sub>5</sub>

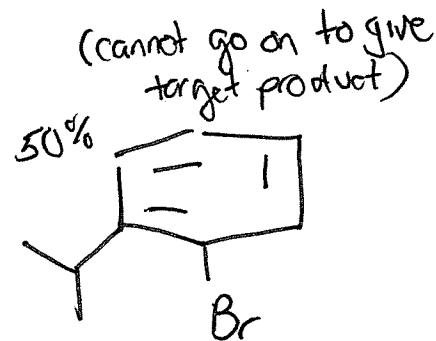
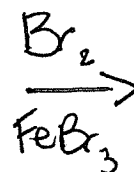
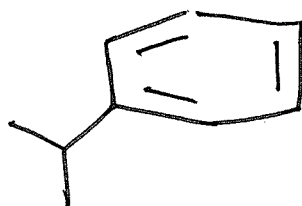


+

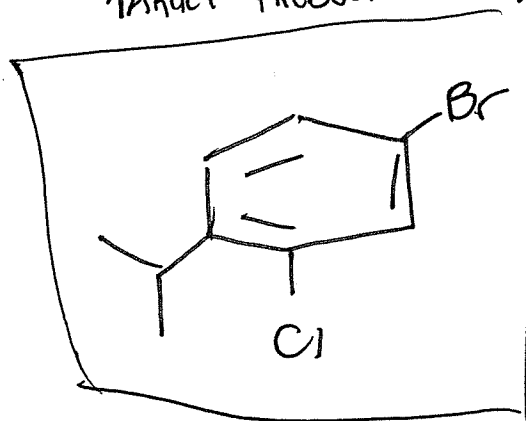


NEITHER OF THESE  
PRODUCTS CAN GO  
ON TO FORM THE  
TARGET PRODUCT

II.

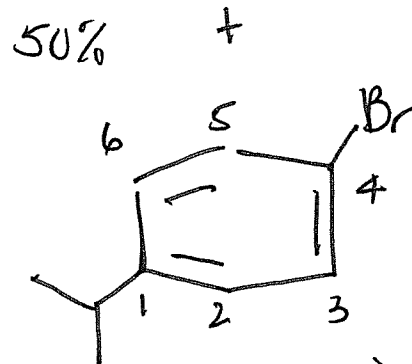
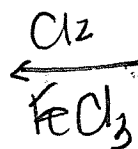


TARGET PRODUCT



REACTION FOLLOWS ACTIVATOR

✓ This product  
represents 50%  
of overall  
theoretical  
yield.

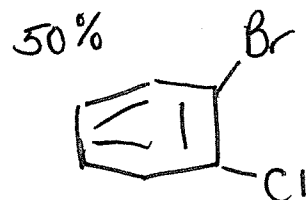
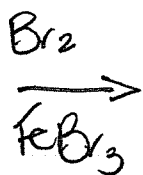


ISOPROPYL  
(ACTIVATOR) DIRECTS TO C<sub>2</sub>, C<sub>6</sub> (same)

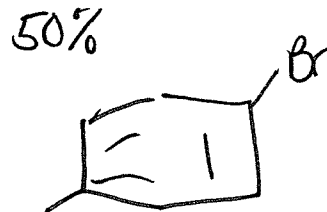
Br  
(DEACTIVATOR) DIRECTS TO C<sub>3</sub>, C<sub>5</sub>

8. (CONT'D)

IV.



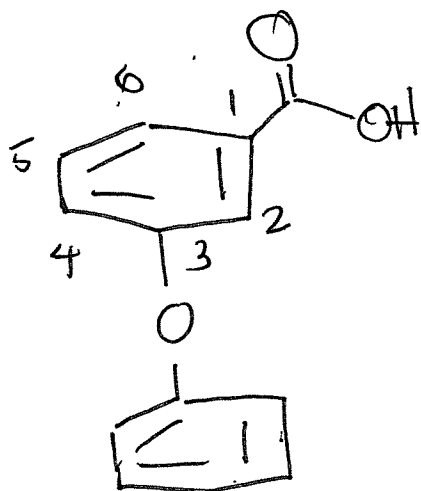
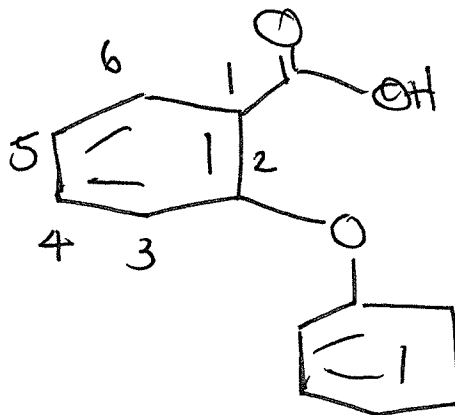
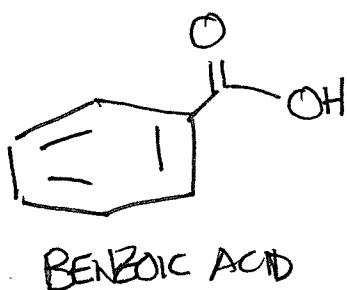
+



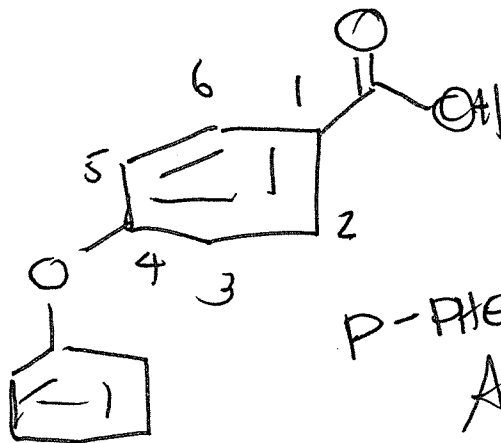
Neither of these products can go on to give the target product.

(C)

9.



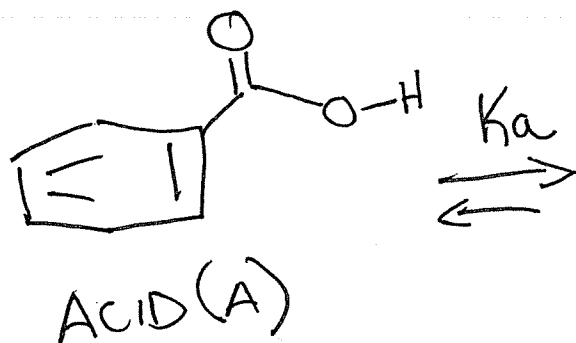
m-PHENOLY BENZOIC ACID



p-PHENOLY BENZOIC ACID

# 9. (CONT'D)

In order to understand the substituent effects on pKa of benzoic acid, consider the following:

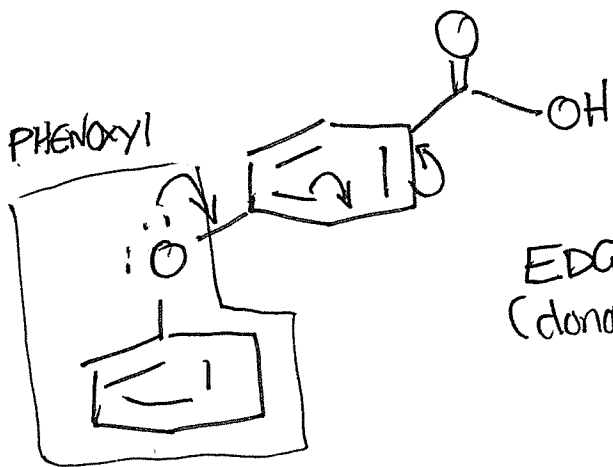


$$K_a = \frac{[CB]}{[A]}$$

$$pK_a = -\log K_a$$

Substituents can make the ring  $\oplus$  or  $\ominus$  by RESONANCE EFFECTS or INDUCTIVE EFFECTS

For a PHENOXY SUBSTITUENT



EDG by RESONANCE: Atom directly bonded to ring has lone pair (donates INTO Ring)

$\uparrow \ominus$  ring  $\uparrow pK_a$

The CB has a  $\ominus$  charge  
If the ring is  $\oplus$  due to substituents, the CB IS STABILIZED

$\oplus \ominus$  STABILIZE CB  
 $\uparrow [CB] \uparrow K_a \downarrow pK_a$

If the ring is  $\ominus$  due to substituents, the CB IS DESTABILIZED

$\ominus \ominus$  DESTABILIZE CB  
 $\downarrow [CB] \downarrow K_a \uparrow pK_a$

# 9. (CONT'D)

The phenoxy group is

EWG by INDUCTION: Atom directly bonded to ring is MORE electronegative than carbon

↑ ⊕ ring    ↓ pKa

So, phenoxy substituted benzoic acids with

• pKa HIGHER than benzoic acid ↑ ⊖ of ring and are EDG by RESONANCE

• pKa LOWER than benzoic acid ↑ ⊕ of ring and are EWG by INDUCTION

o-	m-	pKa <u>BENZOIC ACID</u>	pKa <u>p-PHENOXY BENZOIC ACID</u>
3.53	3.95	4.19	4.52

┌──────────────────┐  
LOWER

EWG by INDUCTION

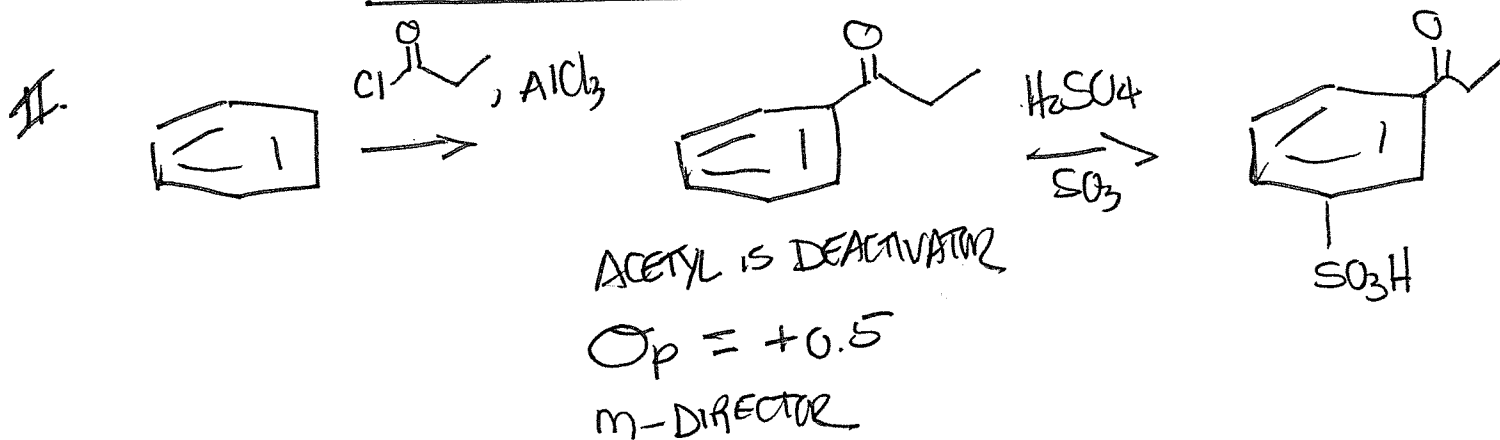
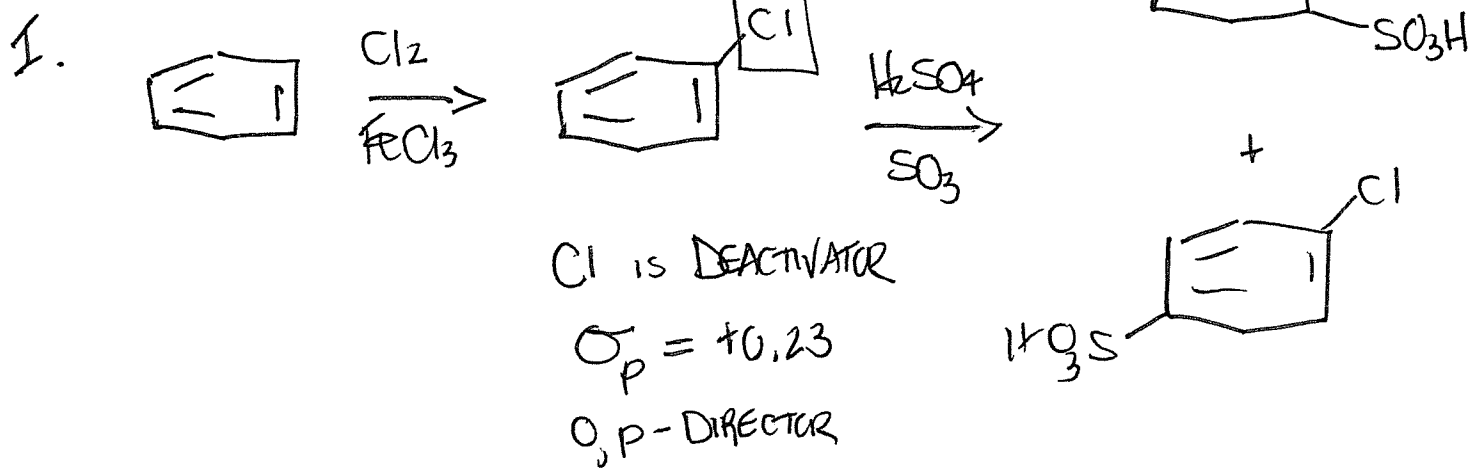
┌──────────────────┐  
HIGHER

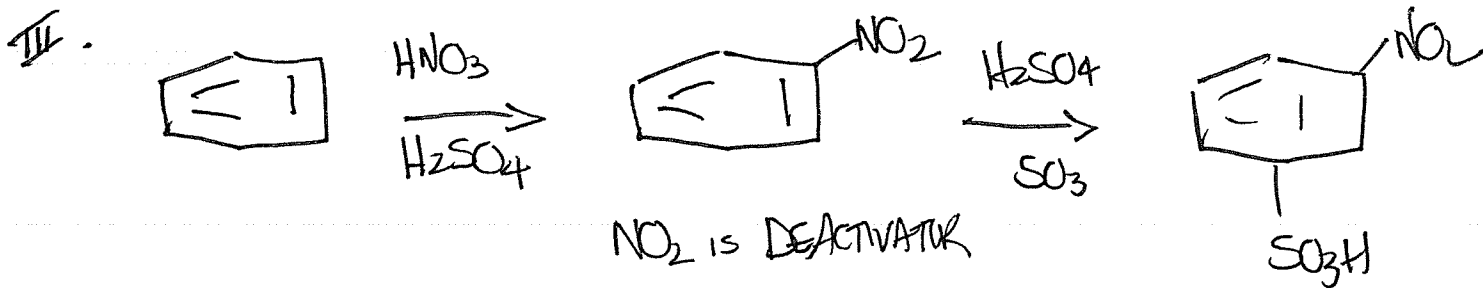
EDG by RESONANCE

So, phenoxy substituent follows an INDUCTIVE EFFECT in ORTHO, META positions, and a RESONANCE EFFECT in PARA position



10. Reaction of benzene with each of the different reagents in the first step all occur at the SAME rate. However, once the substituent is introduced (i.e. Cl for I;  $\text{CH}_3\text{CO}$  for II;  $\text{NO}_2$  for III) the second step rates will be different, based on how the substituent  $\uparrow$  or  $\downarrow$   $\ominus$  character of the ring. The most  $\ominus$  ring (or least  $\oplus$ ) will react fastest in step 2.

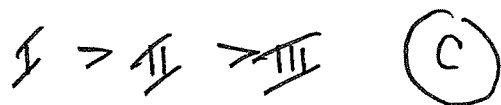




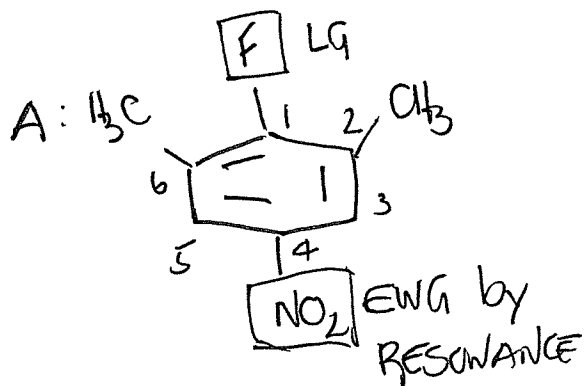
NO<sub>2</sub> is DEACTIVATOR

$$\sigma_p = +0.78$$

m-DIRECTOR



II.



EAS: must have AT LEAST ONE unsubstituted carbon on benzene (i.e. bonded to H) that is not BETWEEN two substituted carbons

NAS: must have leaving group (LG) (usually F) and an EWG by resonance ortho- or para- to the LG

EAS CANNOT occur since "open" carbons @ C<sub>3</sub> and C<sub>5</sub> are between two substituted carbons (STERICALLY BLOCKED)

BENZYLNE: must have LG and at least one ortho H

NAS CAN occur since F leaving group is PARA to NO<sub>2</sub> (EWG by resonance)

$$A = I$$

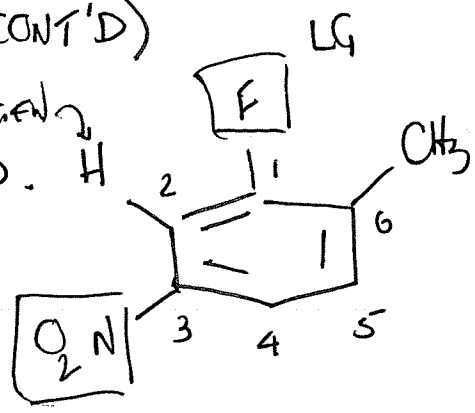
BENZYLNE CANNOT occur since no ortho H relative to carbon bonded to F leaving group



II. (CONT'D)

ORTHO HYDROGEN

B. H



EWG by RESONANCE

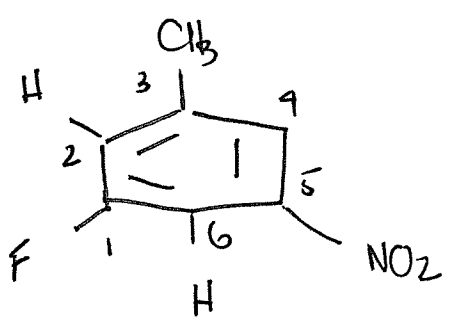
EAS CAN occur  
C4 and C5 are open

NAS CANNOT occur since LG is META to EWG by resonance

BENZYNE CAN occur since ortho Hydrogen is available relative to F LG

B = II, III

C.



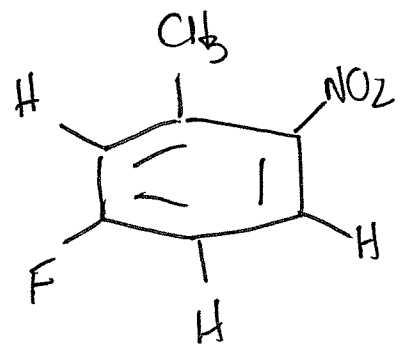
EAS CANNOT occur  
C2, C4, C6 STERICALLY BLOCKED

NAS CANNOT occur since LG is meta to EWG by resonance

Benzyne CAN occur since there is an ortho H relative to LG

C = III

D.



EAS CAN occur

NAS CAN occur

BENZYNE CAN occur

D = I, II, III

A = I

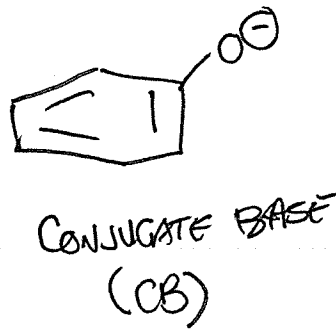
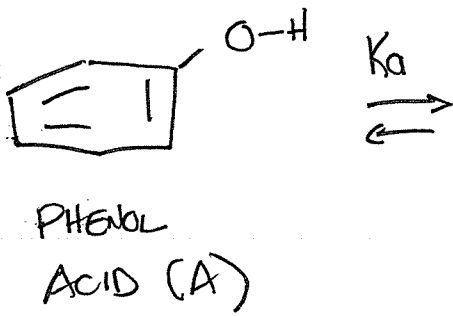
B = II, III

C = III

D = I, II, III

(A)

12.



$$K_a = \frac{[CB]}{[A]}$$

$$pK_a = -\log K_a$$

↓ pKa STRONGEST ACID

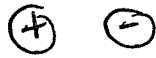
⊕ or ⊖ Ring depends on substituents  
 Substituents w/ largest ⊕  
 σ value ⇒ strongest acid

IF CB IS STABILIZED by making ring ⊕,  
 ↑ [CB] ↑ Ka ↓ pKa  
 STRONGER ACID

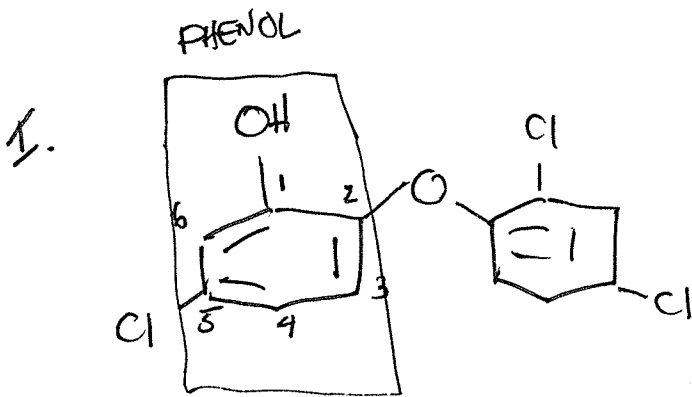
STRONGEST ACID  
 MOST ⊕  
 (or LEAST ⊖)  
 RING

Substituents w/ largest ⊖  
 σ value ⇒ weakest acid

IF CB IS DESTABILIZED by making ring ⊖  
 ↓ [CB] ↓ Ka ↑ pKa  
 WEAKER ACID

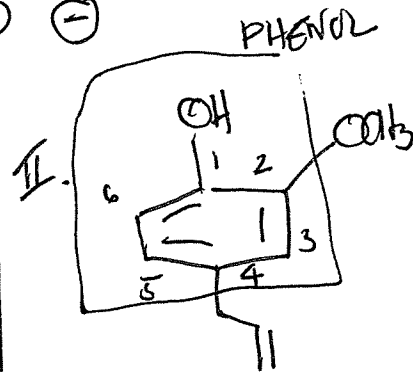


σ<sub>p</sub>/σ<sub>m</sub> determined based on position of substituent relative to phenol OH group



C<sub>2</sub> Phenoxy (ortho) σ<sub>p</sub> = -0.21

C<sub>5</sub> Cl σ<sub>m</sub> = +0.37  
+0.16

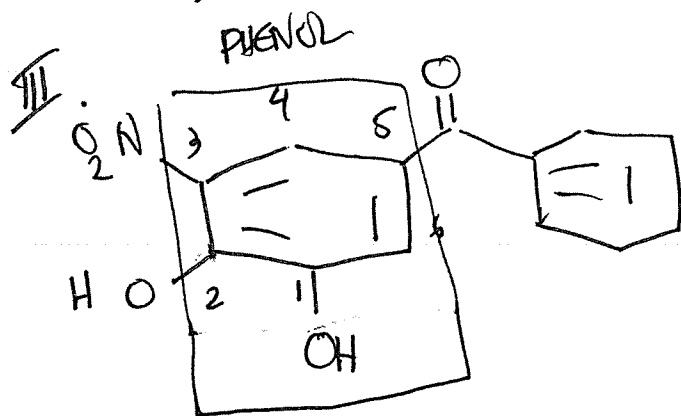


C<sub>2</sub> Methoxy (ortho) σ<sub>p</sub> = -0.27

C<sub>4</sub> CH<sub>3</sub> σ<sub>p</sub> = -0.17

-0.44

12. (CONT'D)



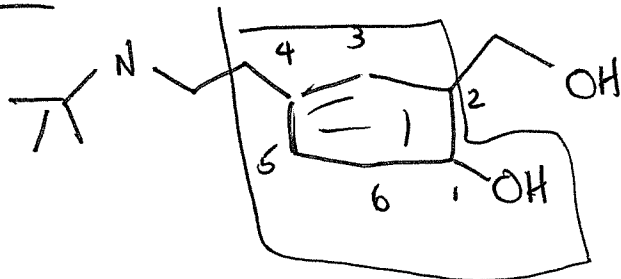
C<sub>2</sub> Hydroxy (ortho)  $\sigma_p = -0.37$

C<sub>3</sub> Nitro  $\sigma_m = +0.71$

C<sub>5</sub> Acetyl  $\sigma_m = +0.38$

**+0.72**

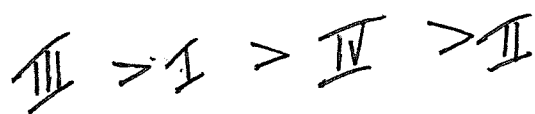
IV.



C<sub>2</sub> CH<sub>3</sub> (ortho)  $\sigma_p = -0.17$

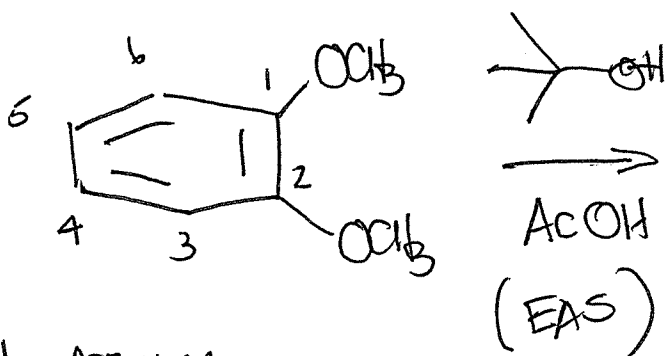
C<sub>4</sub> CH<sub>3</sub>  $\sigma_p = -0.17$

**-0.34**



(E)

13.

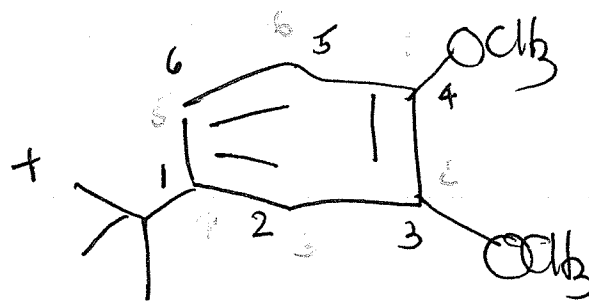
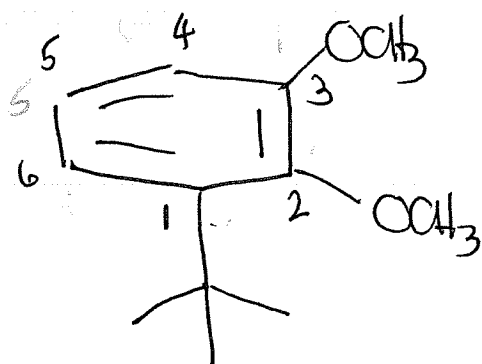


C<sub>1</sub> OCH<sub>3</sub> ACTIVATOR  
o,p-DIRECTOR DIRECTS TO  
C<sub>4</sub>, C<sub>6</sub>

t-Bu at C<sub>6</sub> is SAME compound  
as t-Bu @ C<sub>3</sub>

C<sub>2</sub> OCH<sub>3</sub> ACTIVATOR  
o,p-DIRECTOR DIRECTS TO  
C<sub>3</sub>, C<sub>5</sub>

t-Bu @ C<sub>4</sub> SAME compound  
as t-Bu @ C<sub>5</sub>



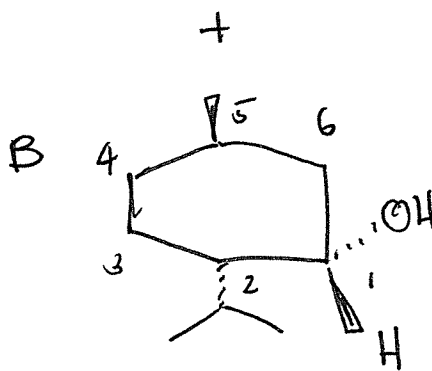
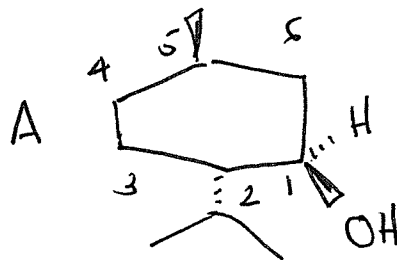
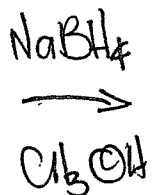
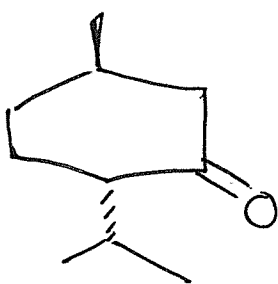
MONOALKYLATED PRODUCTS

1-t-butyl-2,3-dimethoxy benzene

1-t-butyl-3,4-dimethoxy benzene.

(E)

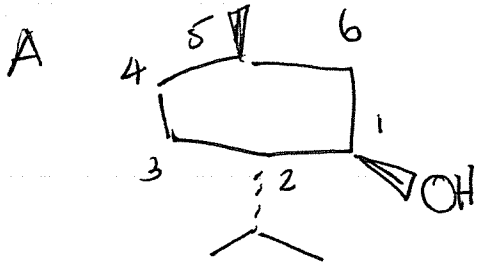
14.



Each of these products has two chair conformations that can be used to predict stability.

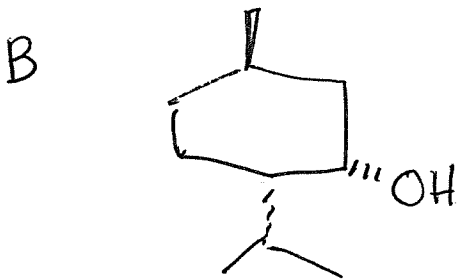
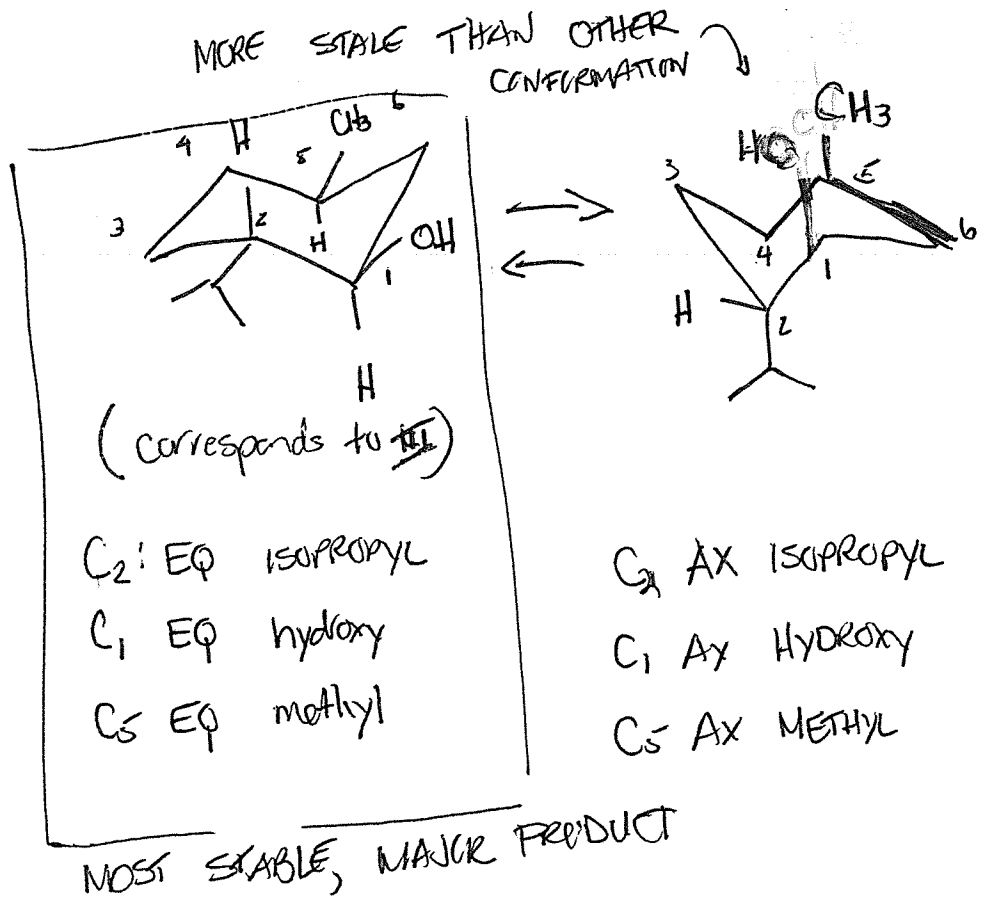
$\text{H}^\ominus$  from  $\text{NaBH}_4$  reacts with menthone from front and back to give rise to two products A and B. These are DIASTEREOMERS and have differ energies (stabilities)

14. (CONT'D)



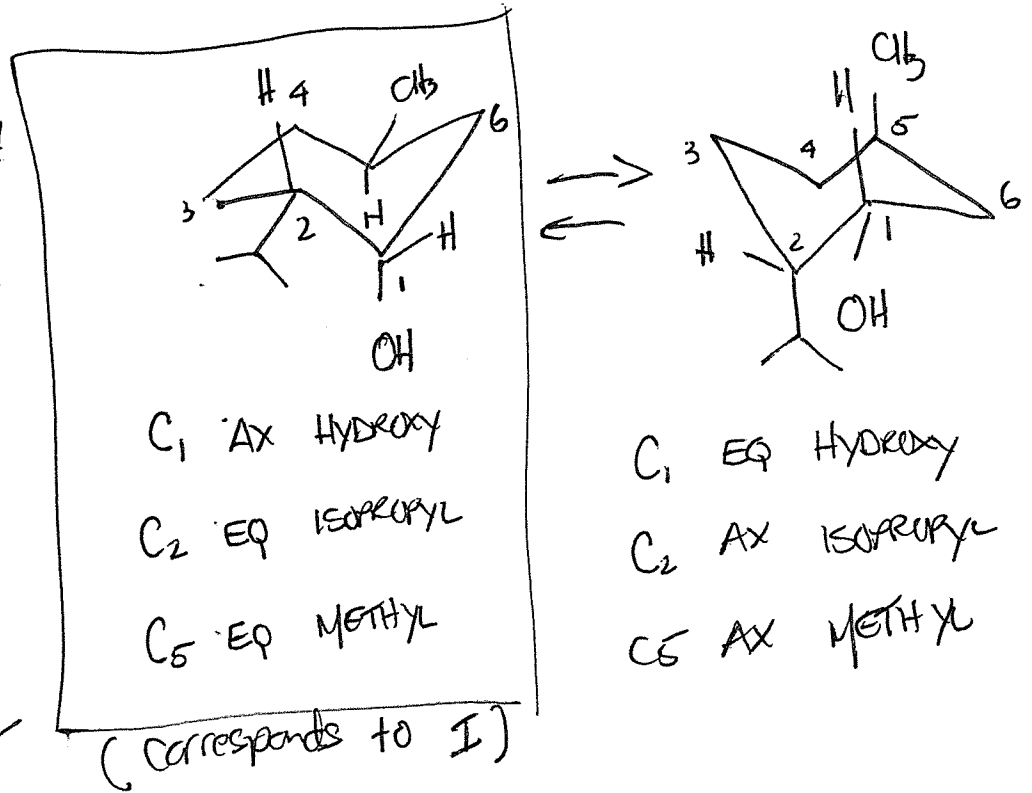
EQ MORE STABLE THAN AXIAL

(-) MENTHOL

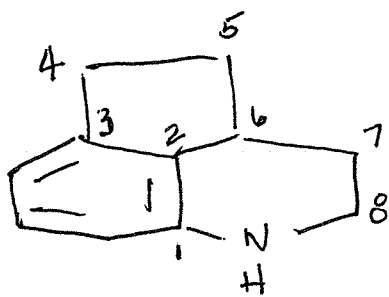


LESS STABLE MINOR PRODUCT

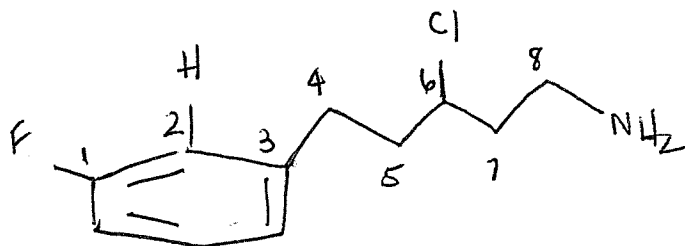
(+) NEOMENTHOL



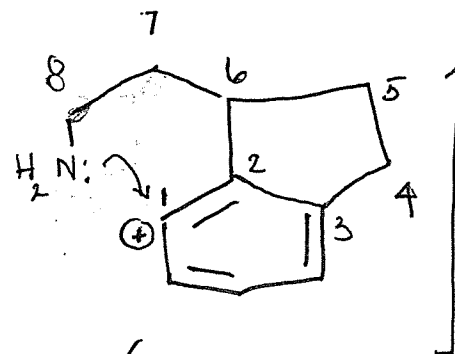
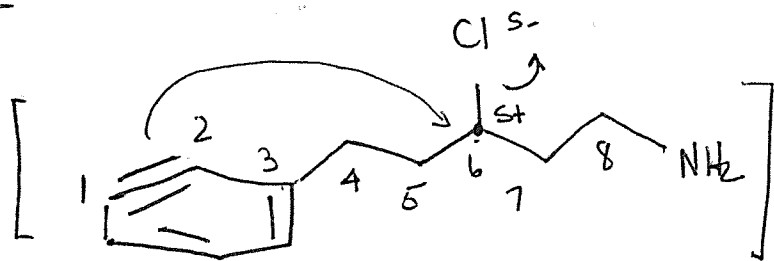
15.



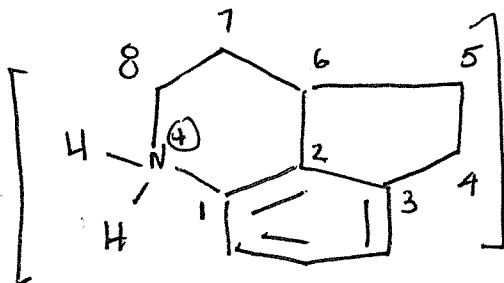
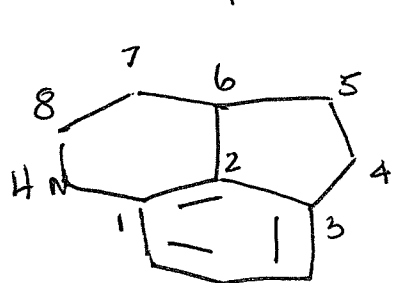
16.



C<sub>2</sub>

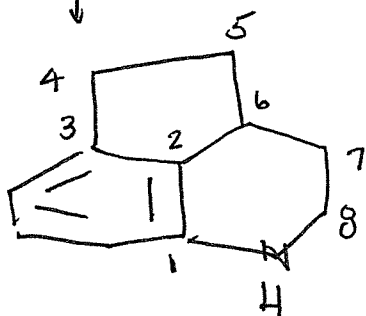


If  $e^-$  from benzyl group react at electrophilic C<sub>6</sub> bonded to Cl

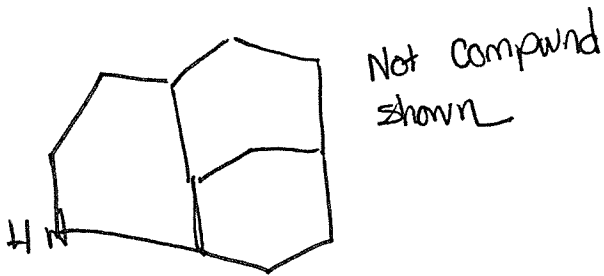
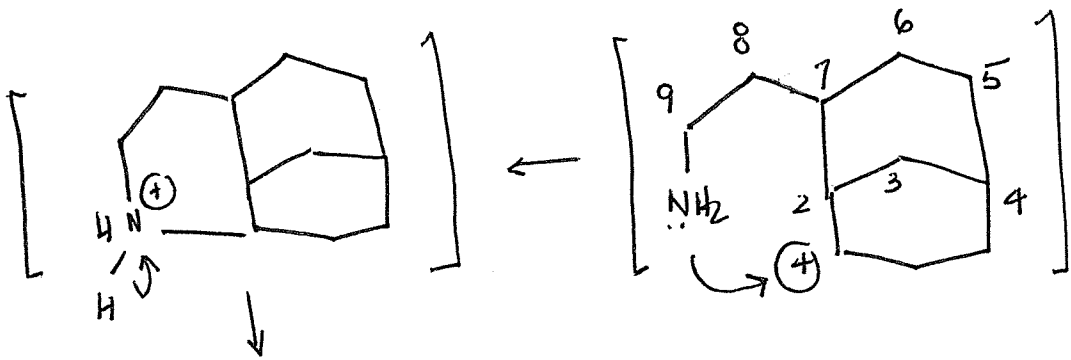
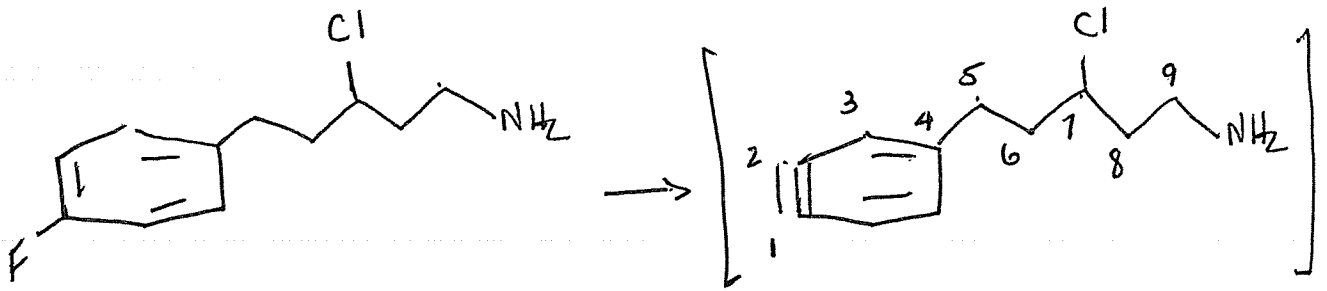


This is the same structure as compound shown

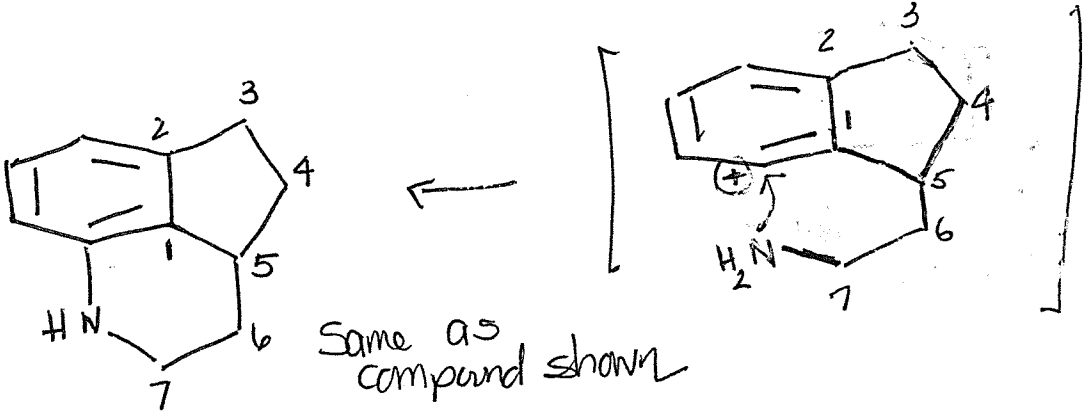
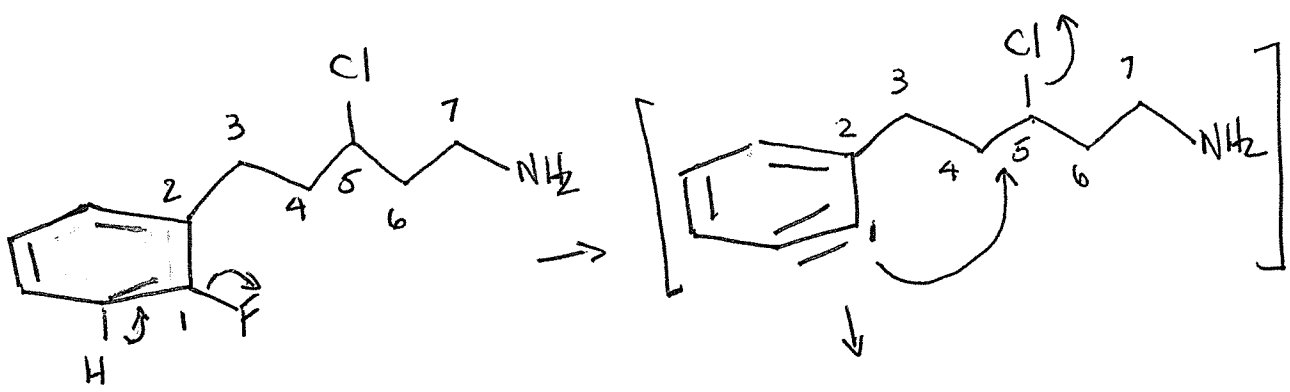
↓ FLIP OVER



II.

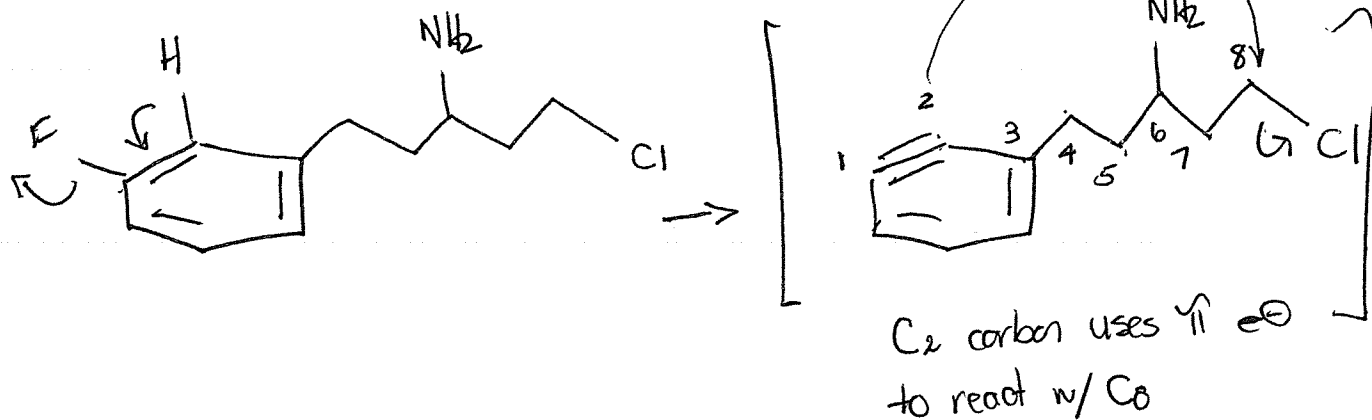


III.



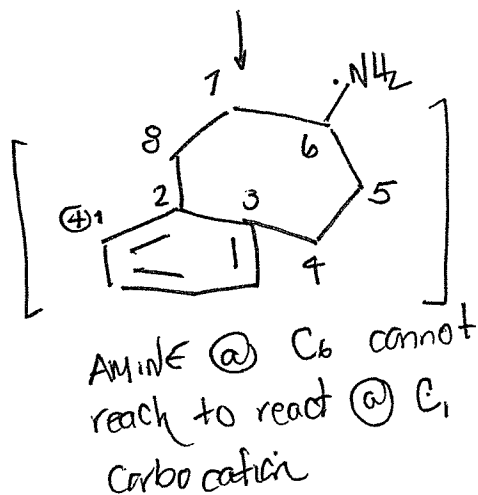
Same as compound shown

IV.

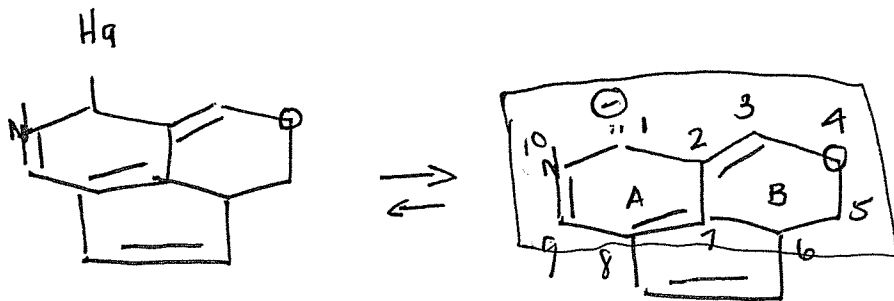


I & III

(B)



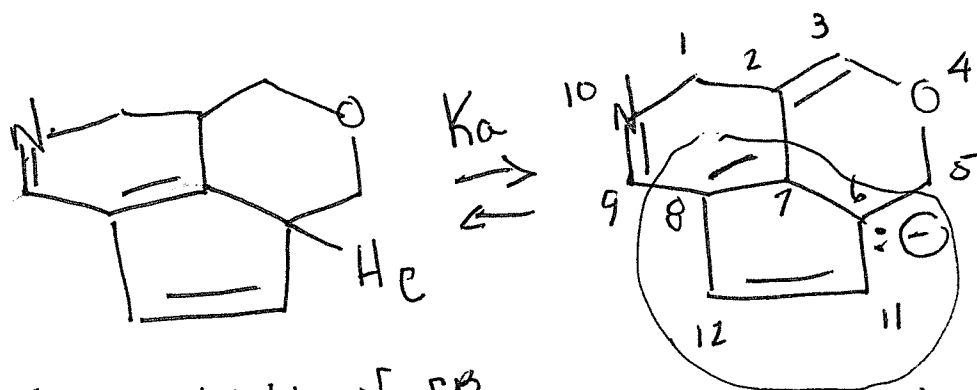
16. I. (FALSE)



The combination of ring A and B of the conjugate base CANNOT be aromatic as C<sub>5</sub> and C<sub>6</sub> are sp<sup>3</sup> and cannot adopt PLANAR geometry required for AROMATICITY



II. The  $pK_a$  of  $H_c$  is lower than the  $pK_a$  of  $H_a$  and  $H_b$  because the conjugate base associated with donation of  $H_c$  is aromatic. When the conjugate base is aromatic, it increases the stability and concentration of the conjugate base, resulting in a much lower  $pK_a$ . (C)



$$K_a = \frac{[CB]}{[A]} \quad \begin{array}{l} \uparrow \text{ stability of CB} \\ \uparrow [CB] \\ \uparrow K_a \quad \downarrow pK_a \end{array}$$

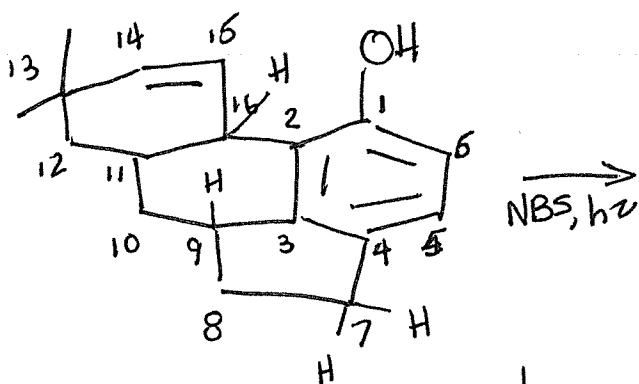
$$pK_a = -\log K_a$$

The five membered ring (circled) is aromatic where the conjugate bases derived from  $H_a$  and  $H_b$  are not.

III. The conjugate base (circled) has both  $e^-$ . The lone pair and the two  $e^-$  from each of the two  $\pi$  bonds in this ring (i.e.  $C_{11}-C_{12}$  and  $C_7-C_8$ ) (TRUE)

IV. Compound A is NOT aromatic as none of the individual rings or combinations fulfill the criteria for aromaticity. (FALSE)

17. Most stable radical forms the fastest in the propagation step of NBS, h $\nu$  reaction

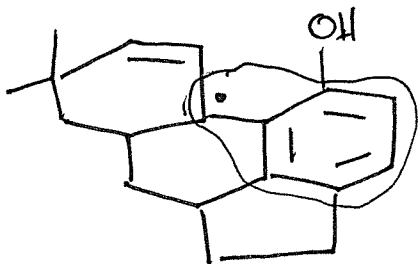


$3^\circ > 2^\circ > 1^\circ$   
MOST STABLE      LEAST STABLE

Benzylic bromination reaction  
Benzylic hydrogen at C7, C9, C16

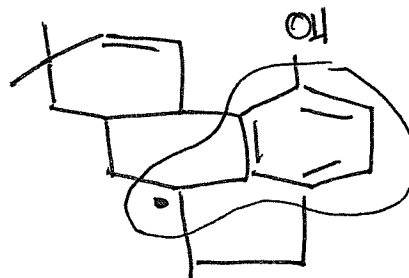
(B)

I. MOST STABLE



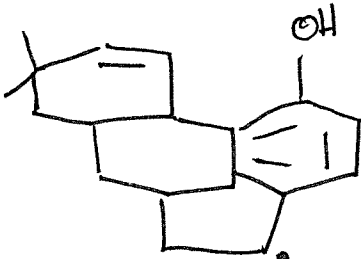
3° BENZYLIC RADICAL  
(also ALLYLIC)

II.



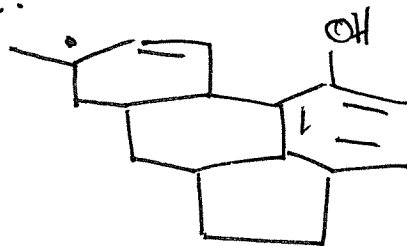
3° BENZYLIC RADICAL

III.



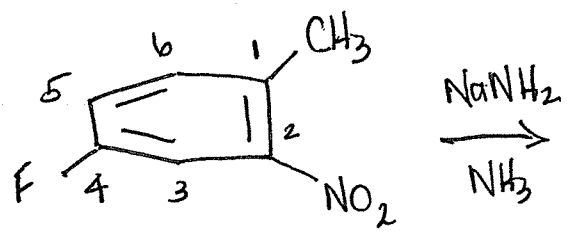
2° BENZYLIC RADICAL

IV.



NOT BENZYLIC  
RADICAL  
3° ALLYLIC

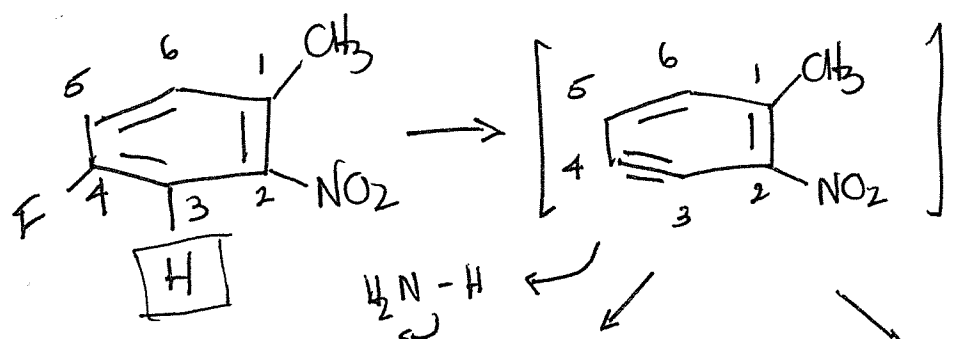
18.



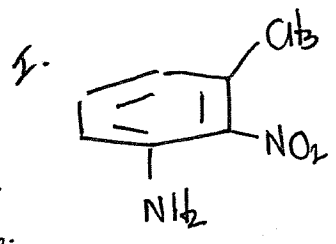
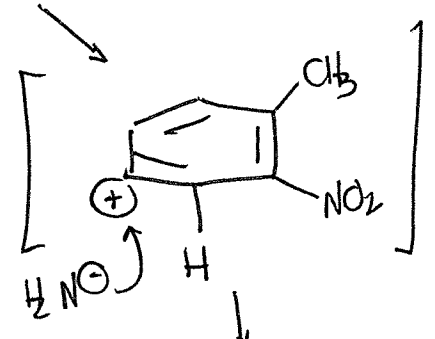
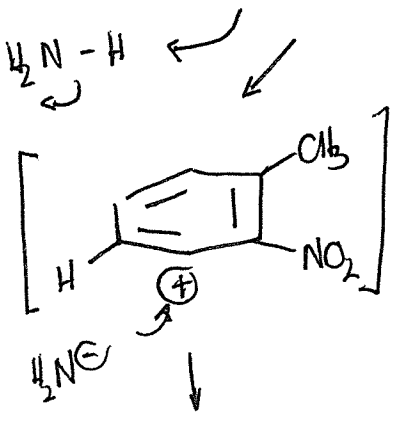
4-FLUORO-2-NITRO  
TOLUENE

BENZYNE REACTION

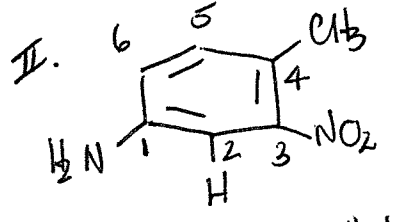
There are two ortho hydrogens.  
Must consider products from BOTH  
ortho hydrogens



C3 ORTHO  
HYDROGEN



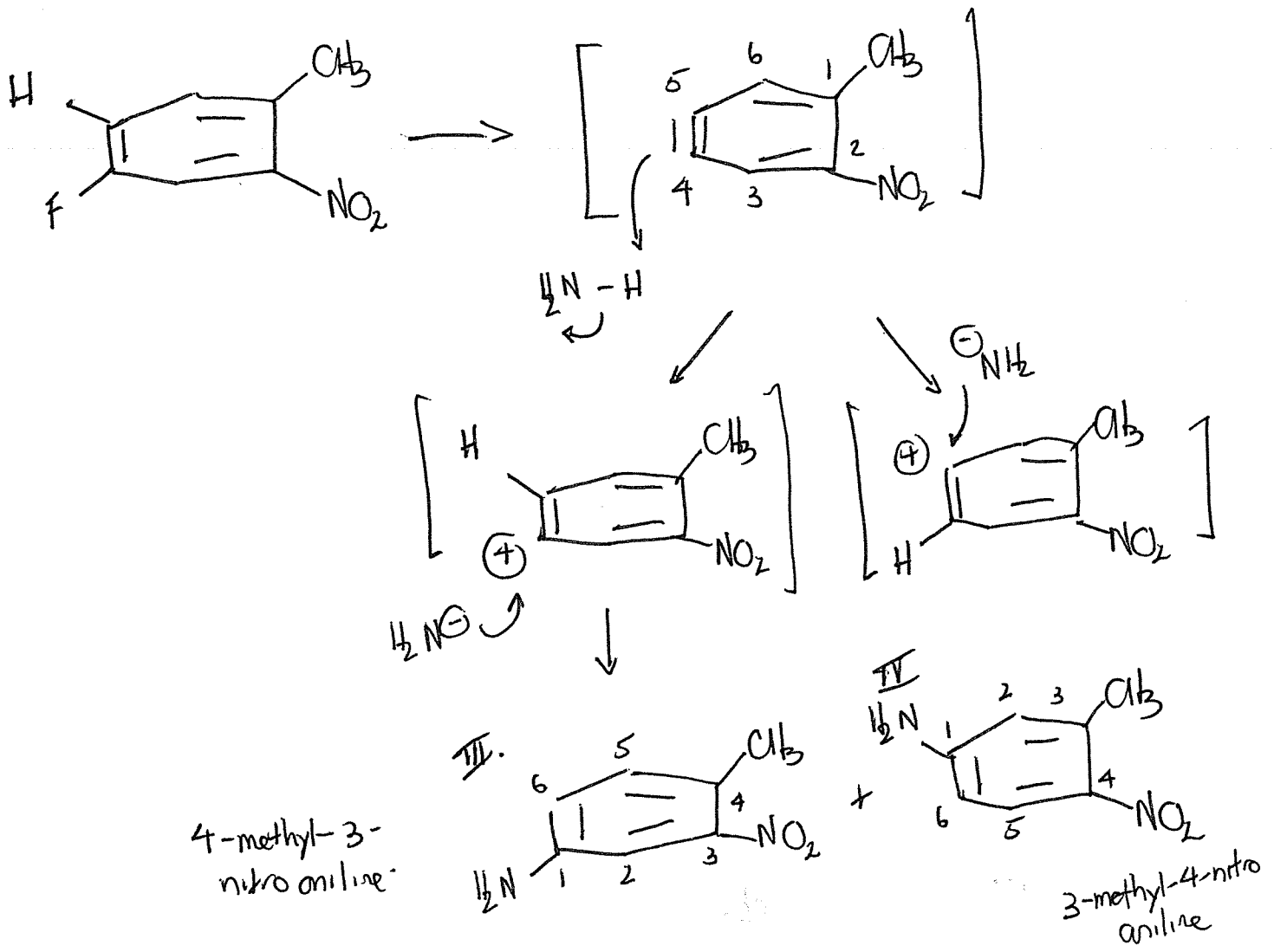
3-methyl-2-nitroaniline



4-methyl-3-nitroaniline

ALSO NEED TO CONSIDER C5 ORTHO HYDROGEN

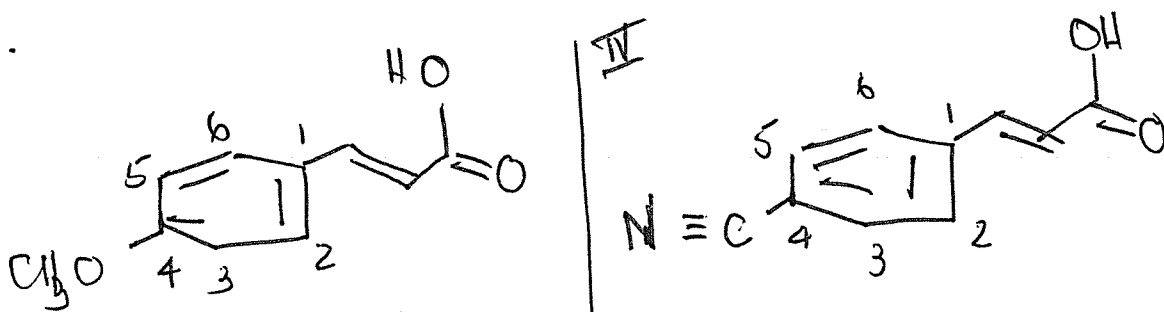
18. (CONT'D)



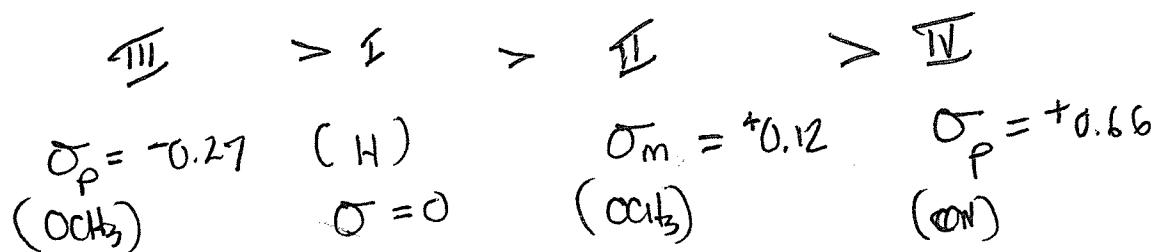
The overall yield of the reaction, from both the C<sub>3</sub> AND C<sub>5</sub> ortho hydrogens, is 25% I, 25% II, 25% III and 25% IV. But II and III are exactly the same compound. so there is 50% of this compound which is 4-methyl-3-nitro aniline. (II)

(B)

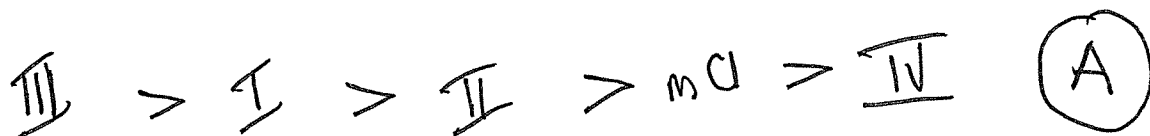
The most potent compound is III and the least potent is IV.



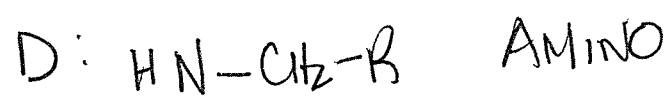
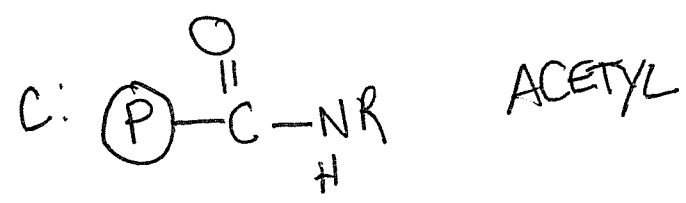
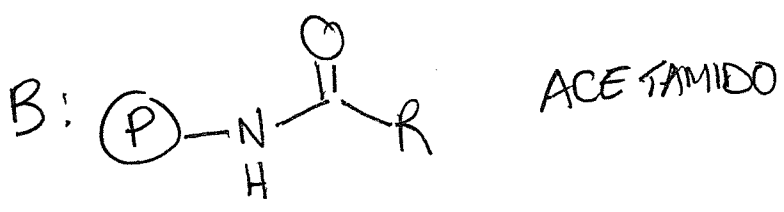
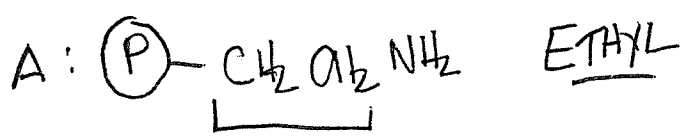
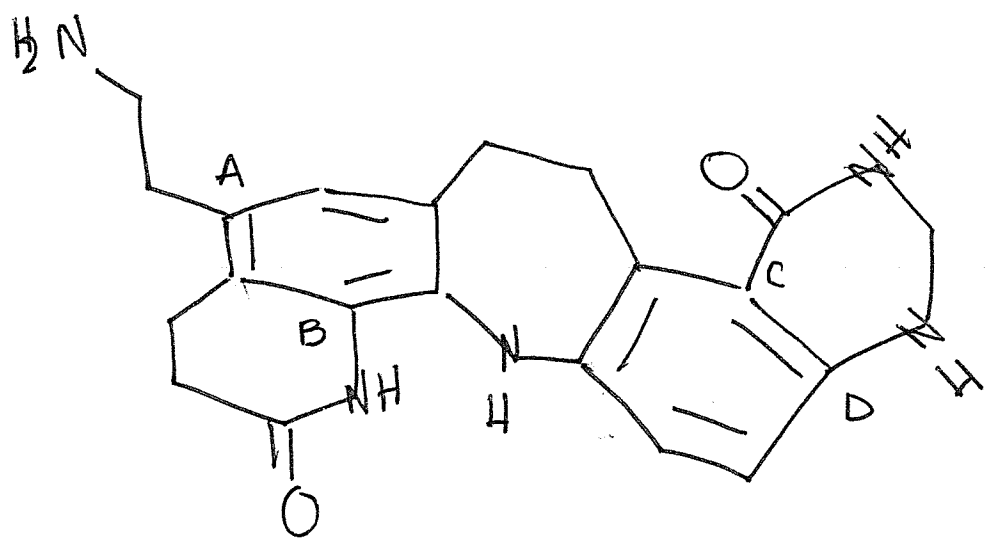
The only difference between these compounds is the substituent @ C<sub>4</sub>. For III, the substituent is an EDG w/ a  $\sigma_p$  value = -0.27 and the cyano group is an EWG with a  $\sigma_p$  value of +0.66. This suggests Rings with ↑ ⊖ character are more potent and rings w/ less ⊖ or more ⊕ character are less potent.



A meta chloro group on the ring would have a  $\sigma_m$  value = +0.37 meaning it would fall between II and IV.



20.

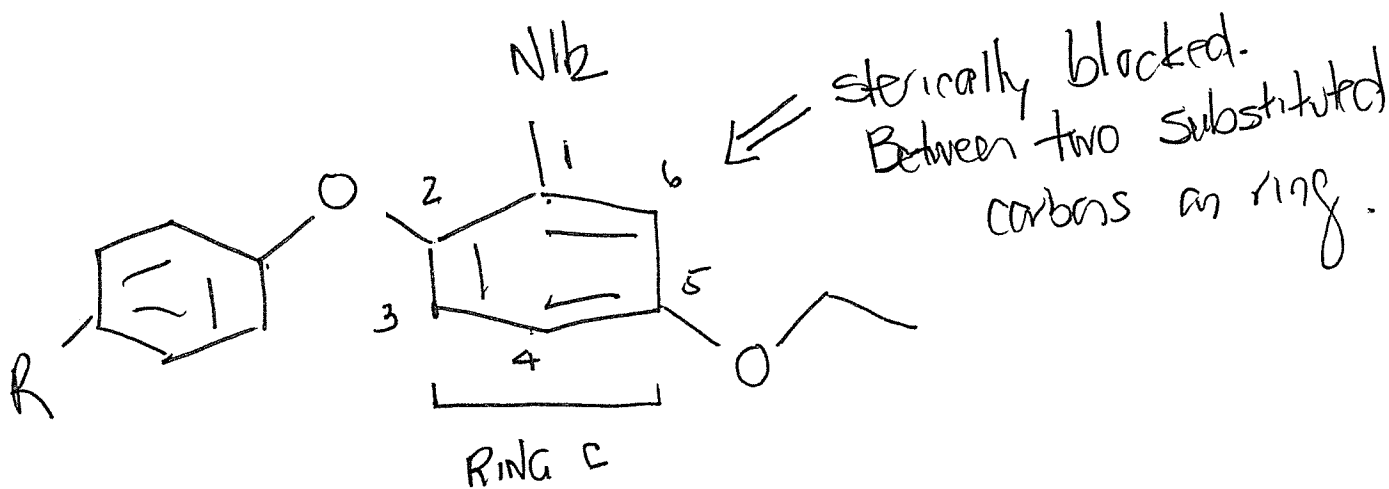


if N of HN-C(=O) bonded to parent

if C of -C(=O)-NH bonded to parent

(D)

Once most activated ring is identified, then consider directing ability of substituents on that ring (i.e. Ring C)



C<sub>1</sub>: AMINO     $\sigma_p^-$     ACTIVATOR     $\sigma_p = -0.66$   
 DIRECTOR  
 DIRECTS TO ~~C<sub>6</sub>~~, C<sub>4</sub>    BUT    C<sub>6</sub> sterically blocked

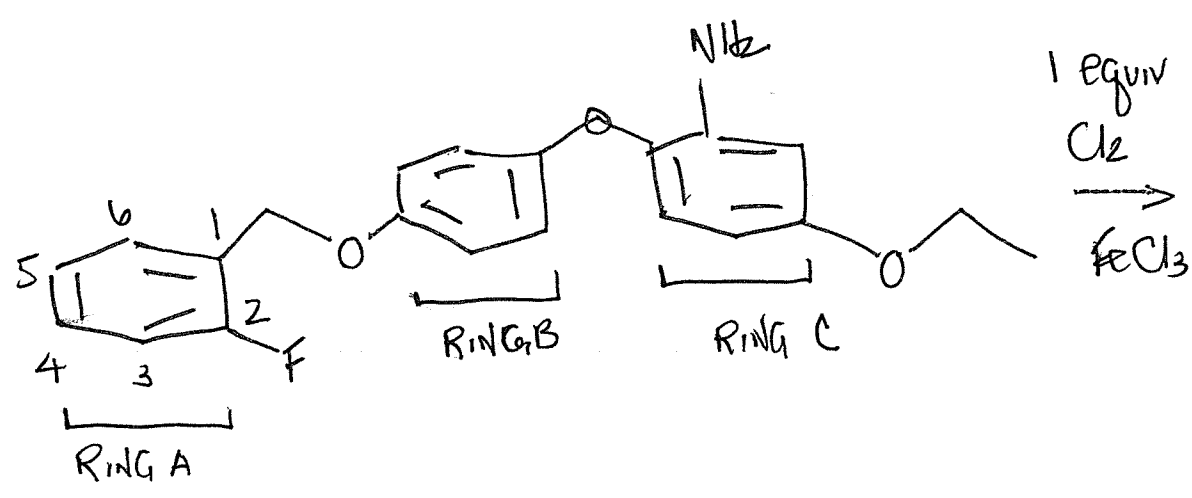
C<sub>2</sub>: PHENOXY     $\sigma_p^-$     ACTIVATOR     $\sigma_p = -0.21$   
 DIRECTOR  
 DIRECTS TO C<sub>3</sub>

C<sub>5</sub>: ETHOXY     $\sigma_p^-$     ACTIVATOR     $\sigma_p = -0.24$   
 DIRECTOR  
 DIRECTS TO C<sub>4</sub>, ~~C<sub>6</sub>~~

Reaction directed to C<sub>4</sub> b/c both ethoxy and amino direct here.

(D)

21.



Consider which of the three rings is most ACTIVATED base on the # of activating / deactivating groups on the ring. The most ACTIVATED (or LEAST DEACTIVATED) ring will react to give major product(s)  
 MOST ACTIVATOR = MOST  $\ominus$  (or least  $\oplus$ )

A:  $\text{P}-\text{F}$  : DEACTIVATOR  $\sigma_p =$

$\text{P}-\text{CH}_3$  : ACTIVATOR  $\sigma_p = -0.17$   
 (METHYL)

B:  $\text{P}-\text{O}-\text{CH}_3$  : ACTIVATOR  
 (METHOXY)

$\text{P}-\text{O}-\text{Ph}$  : ACTIVATOR  
 (PHENOXY)

C:  $-\text{NH}_2$  : ACTIVATOR  
 (AMINO)

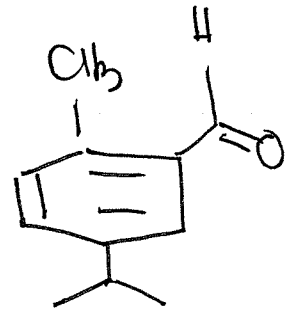
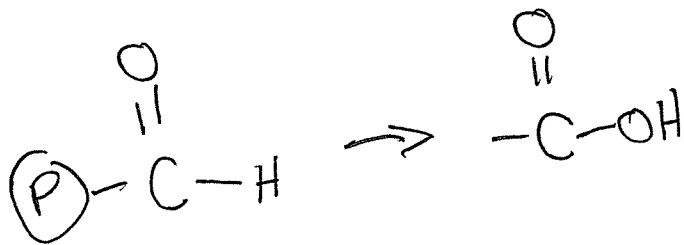
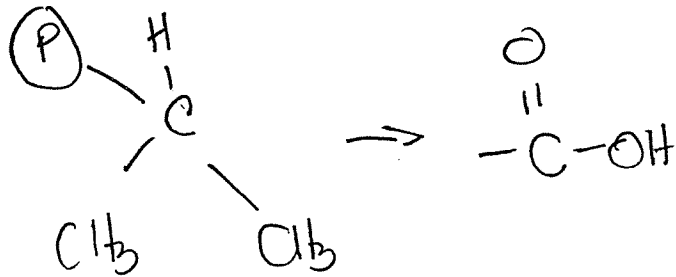
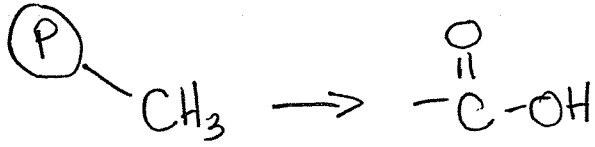
$-\text{O}-\text{CH}_2\text{CH}_3$  : ACTIVATOR  
 (ETHOXY)

$-\text{O}-\text{Ph}$  (PHENOXY) : ACTIVATOR

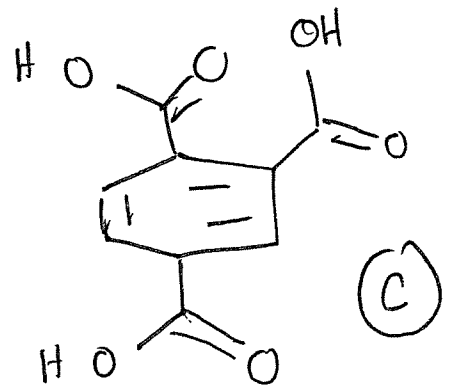
Ring C is MOST ACTIVATED b/c has most activating groups



22.  $KMnO_4$  reacts with benzylic carbons (and N) w/ at least one H, and oxidizes those carbons to carboxylic acids



xs  $KMnO_4$



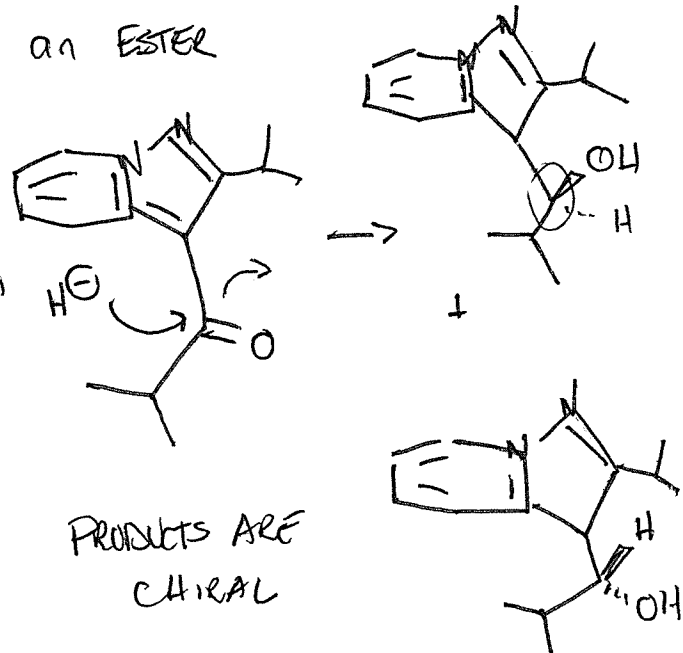
23.  $NaBH_4$ ,  $AlEt_3$  reacts with aldehydes and ketones, but not esters or carboxylic acids.  $NaBH_4$  will not react w/ the carbonyl group in IV b/c it is an ESTER

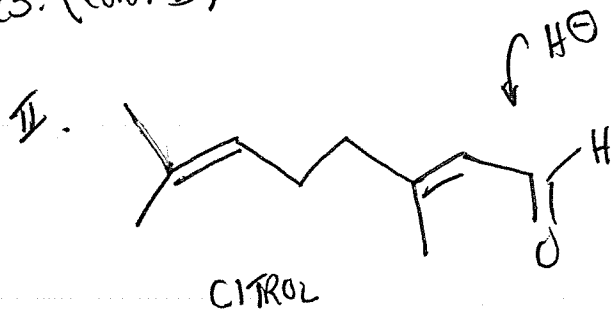
I. Ibuprofen does not contain any chiral centers and is not chiral. The ketone reacts to create a new chiral center

Reacts from TOP and BOTTOM

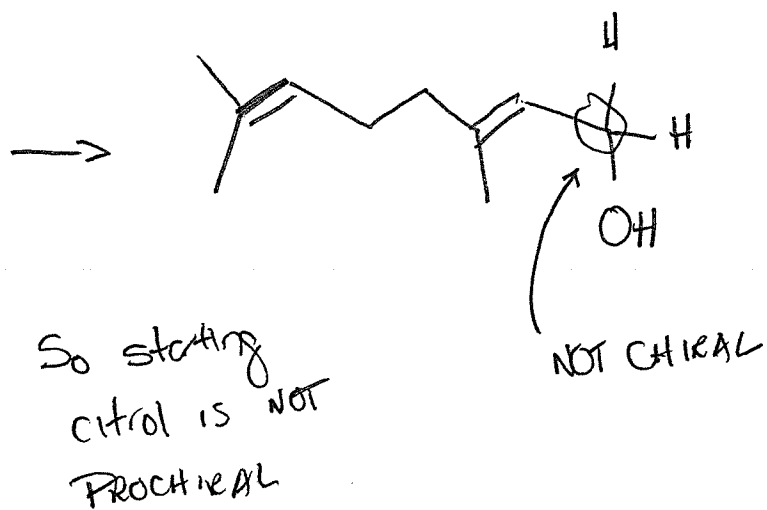
Starting Ibuprofen IS PROCHIRAL

PRODUCTS ARE CHIRAL

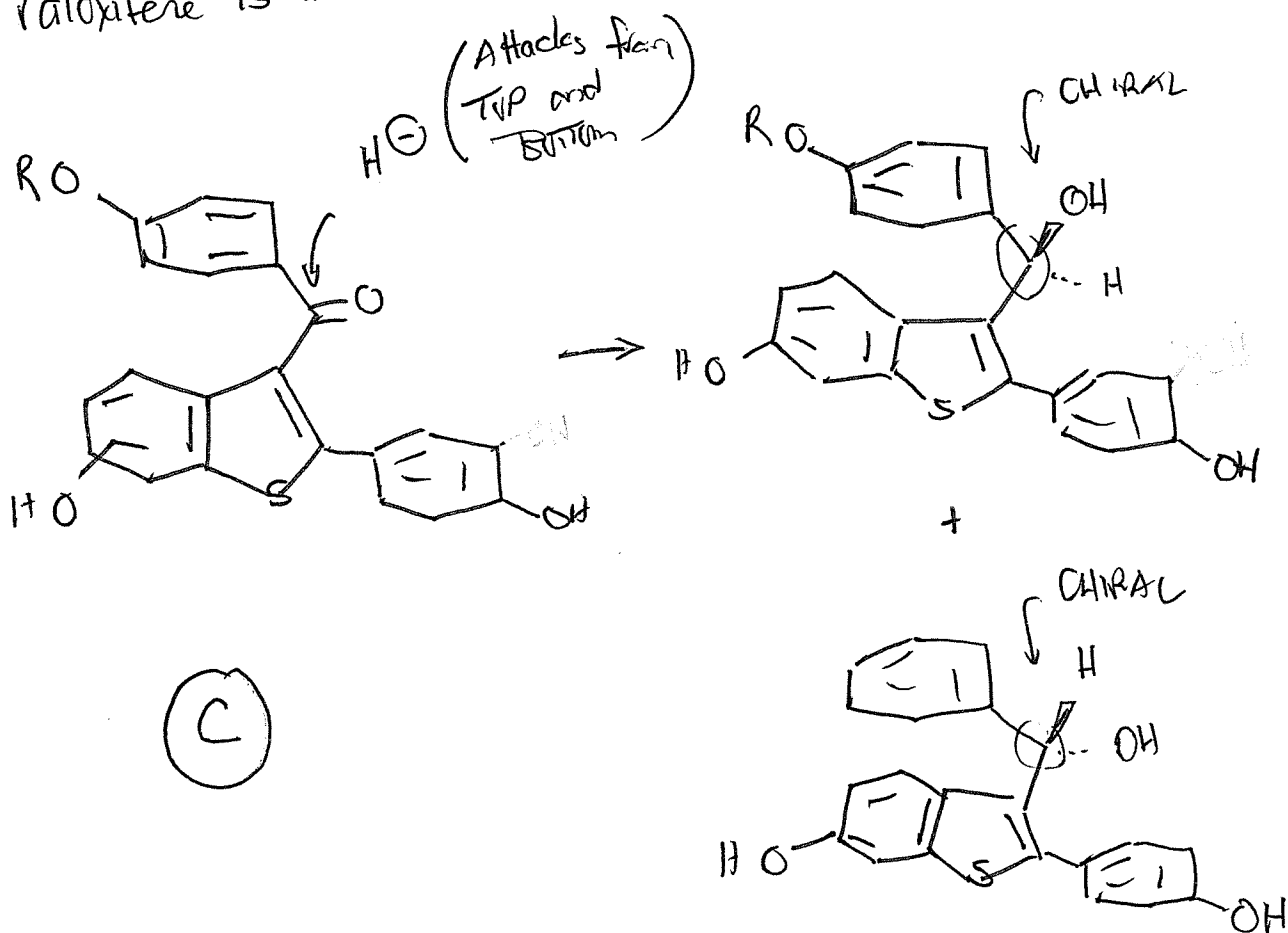




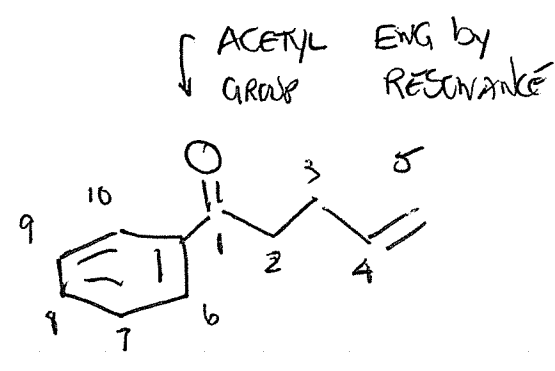
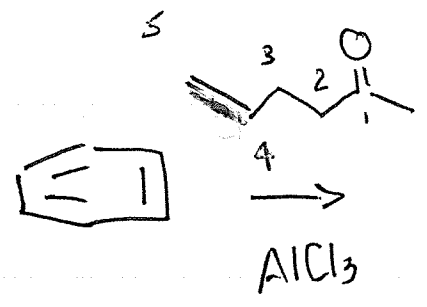
Citral reacts w/  $\text{NaBH}_4$  but does not form a chiral center because the new  $\text{sp}^3$  carbon is not bonded to 4 unique substituents



III. Ketone of raloxifene reacts w/  $\text{NaBH}_4$ . Raloxifene does not contain any chiral centers but reaction w/  $\text{NaBH}_4$  results in formation of a new  $\text{sp}^3$  carbon that is chiral, therefore raloxifene is PROCHIRAL in this reaction.

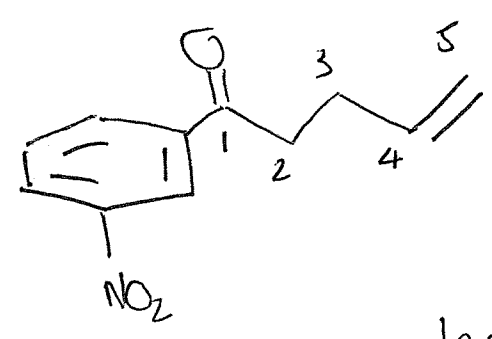


24.



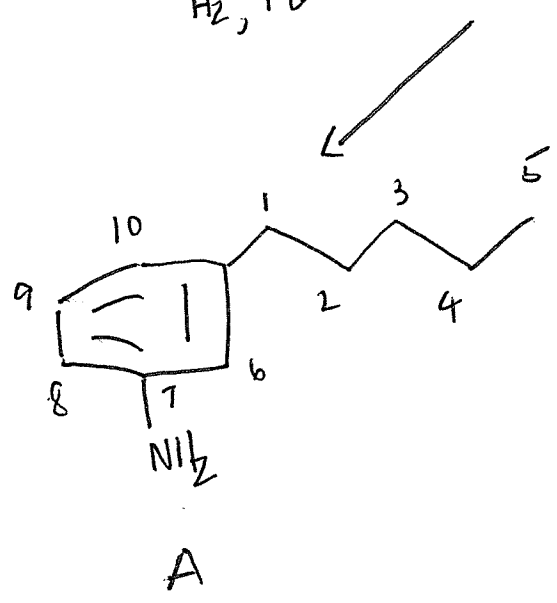
Catalytic hydrogenation  
 ( $H_2, Pt$ ) reduces benzylic  
 $NO_2$ , ketones and  
 alkenes.

$HNO_3, H_2SO_4$

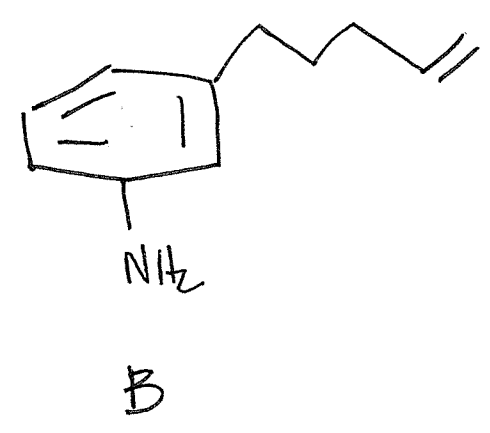


This represents structure X.

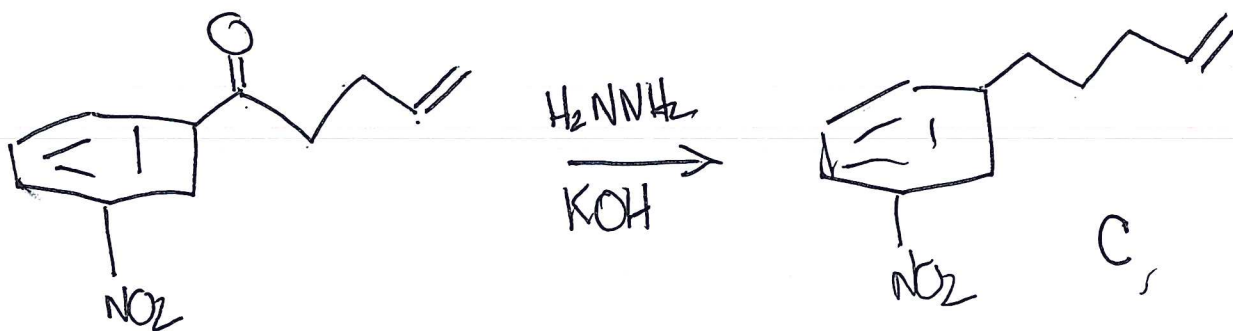
$H_2, Pt$



$Zn(Hg), HCl$



Clemmensen  
 reduction  
 reduces benzylic  
 ketones and  
 nitro groups  
 but NOT  
 alkenes



Wolff-Kishner ( $\text{KOH}$ ,  $\text{H}_2\text{NNH}_2$ )  
 reduces benzylic ketones  
 only, not nitro or  
 alkenes

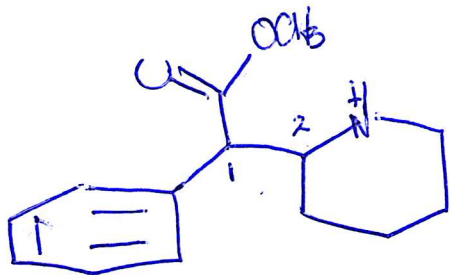
~~A~~ A = III

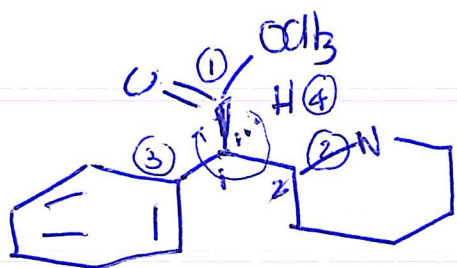
B = II

C = I

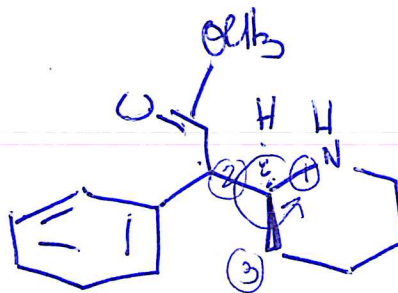
(E)

25. Methylphenidate has 2 chiral centers at  $\text{C}_1$  and  $\text{C}_2$ . There are four stereoisomers of methylphenidate that are shown as I, II, III and IV. Focalin is the d-isomer of the racemic mixture of ritalin. A racemic mixture is a 50:50 mixture of ENANTIOMERS. So ritalin is a mixture of focalin (RR) and its ENANTIOMER (S,S).



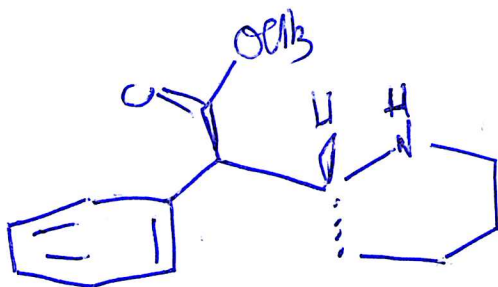


Configuration at  $C_1$  is R  
in this structure



Configuration at  $C_2$   
in this structure is  
S

So R, R is

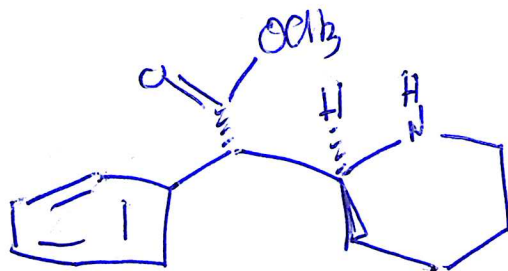


CORRESPONDS TO

IV

(D)

and S, S is



CORRESPONDS TO

I