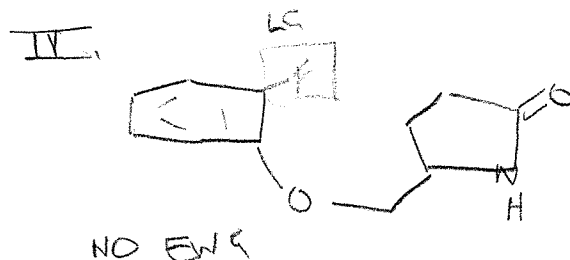
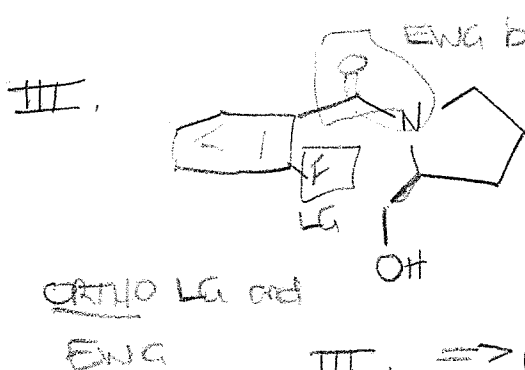
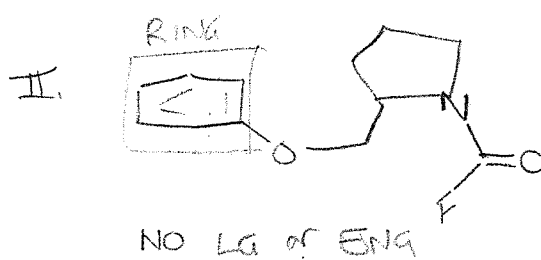
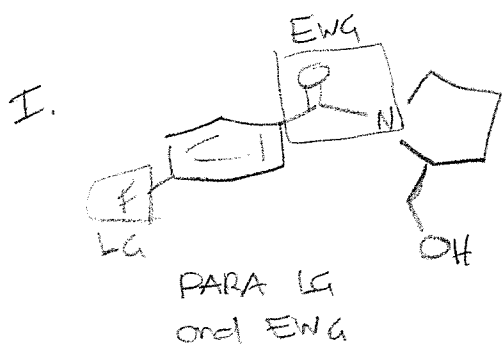


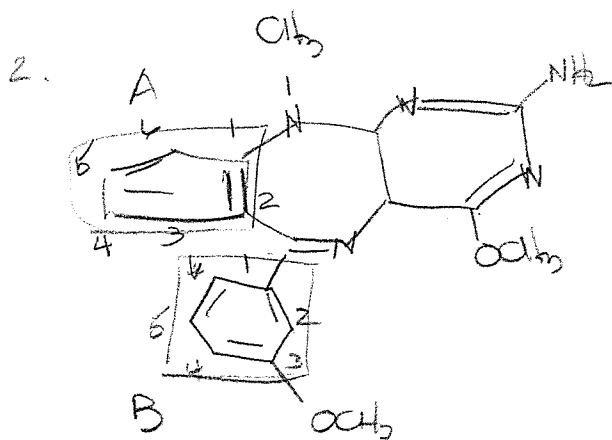
EXAM 3
5/20/17
SOLUTIONS

1. NAS requires: Leaving group on benzene (F, Cl, Br)
AND ortho- or para- electron-withdrawing group by resonance (EWG)
EWG by Resonance: atom directly bonded to ring part of external TP system

Benzodiazepine specifically requires LG and EWG by resonance OR ORTHO

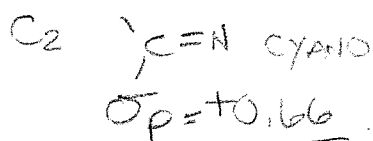
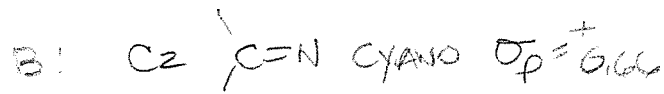
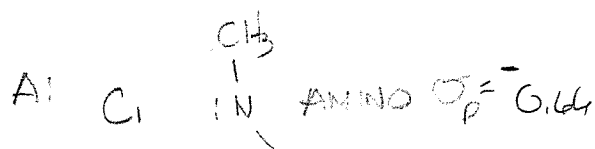


III. => (C)



There are two benzene rings, labeled as A and B.

1st establish which is MOST REACTIVE (i.e. most \ominus) base on most activating groups (or least deactivating)



$\sigma_{\text{sum}} = 0$

$\sigma_{\text{sum}} = 0.39$

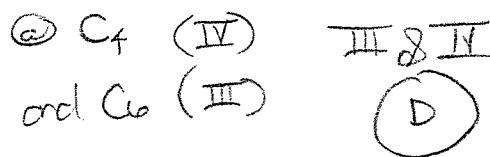
MORE ACTIVATED
(less \oplus)

(\oplus indicates DEACTIVATION)

Then, determining the directing ability of substituents on ring A

C1: AMINO o-director
Directs to C4, C6

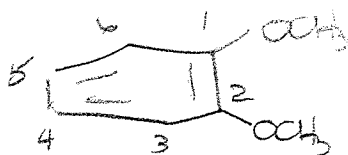
Chlorination reaction occurs



C2: CYANO m-director
Directs to C4, C6

1st alkylation

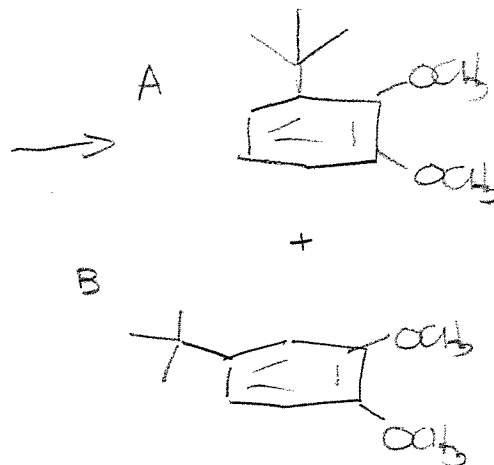
3.



C₁: OCH₃ directs to C₄, C₆

C₂: OCH₃ directs to C₃, C₅

Since both OCH₃ are EQUALLY activating both direct rxn



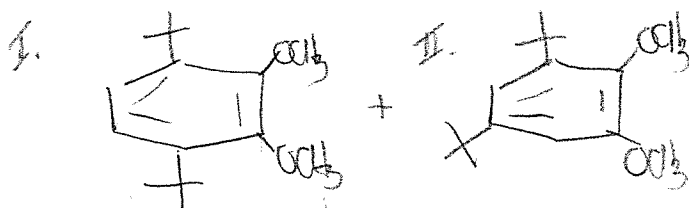
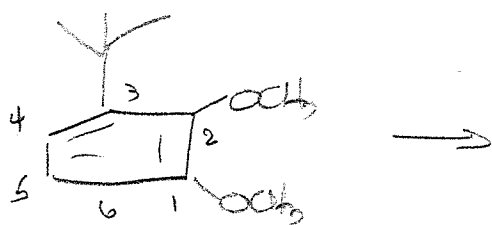
Rxn @ C₆ gives SAME product as rxn @ C₃

Rxn @ C₄ gives SAME product as rxn @ C₅

TWO products form from MONO alkylation

2nd Alkylation

A
MONO
PRODUCT



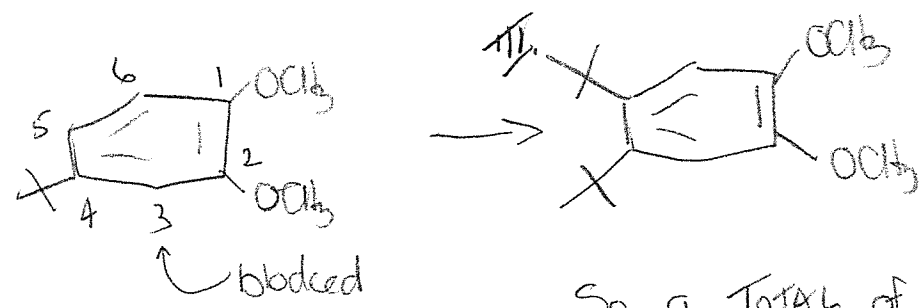
C₁: OCH₃ (A) Directs to C₄, C₆

C₂: OCH₃ (A) Directs to C₅

C₃: — (A) Directs to C₄, C₆

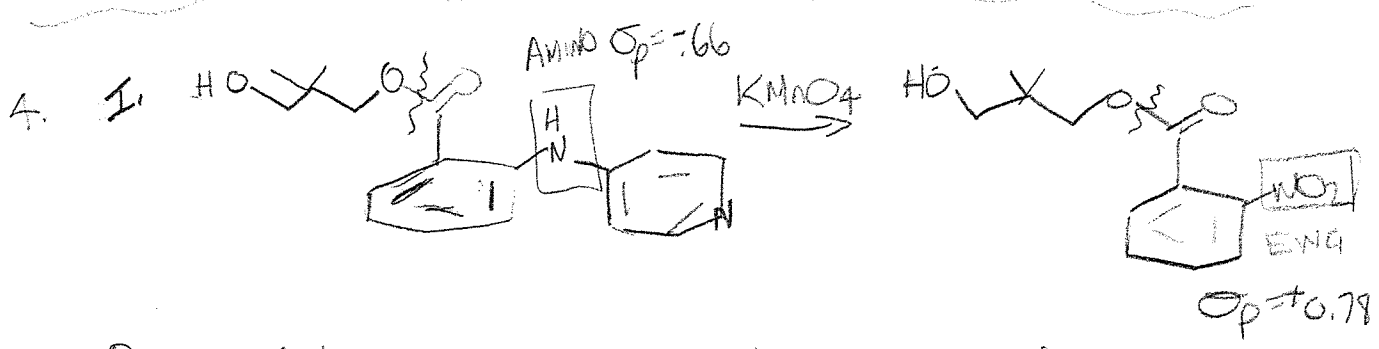
All three substituents are activators. Since OCH₃ and + direct to C₄, C₆, these are MOST activated positions

3. (CONT'D)



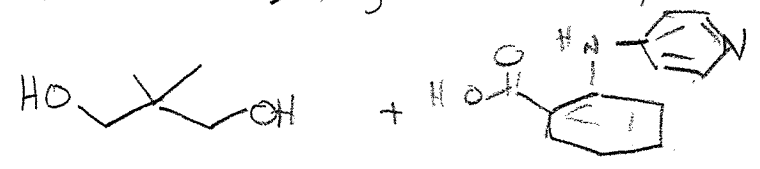
- C₁: (A) Directs to C₆
- C₂: (A) Directs to C₅
- C₄: (A) Directs to C₃

So a TOTAL of 3
 dialkylated products form
 as major products of
 the reaction (C)

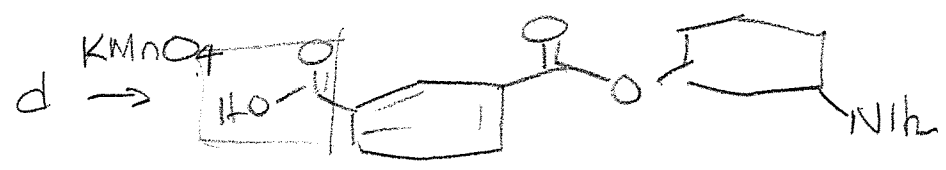
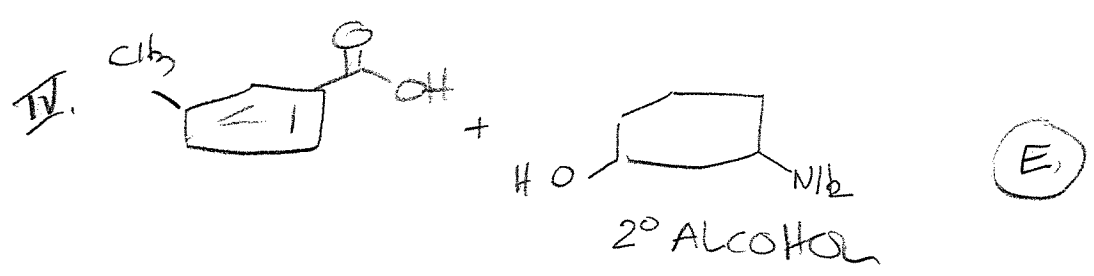
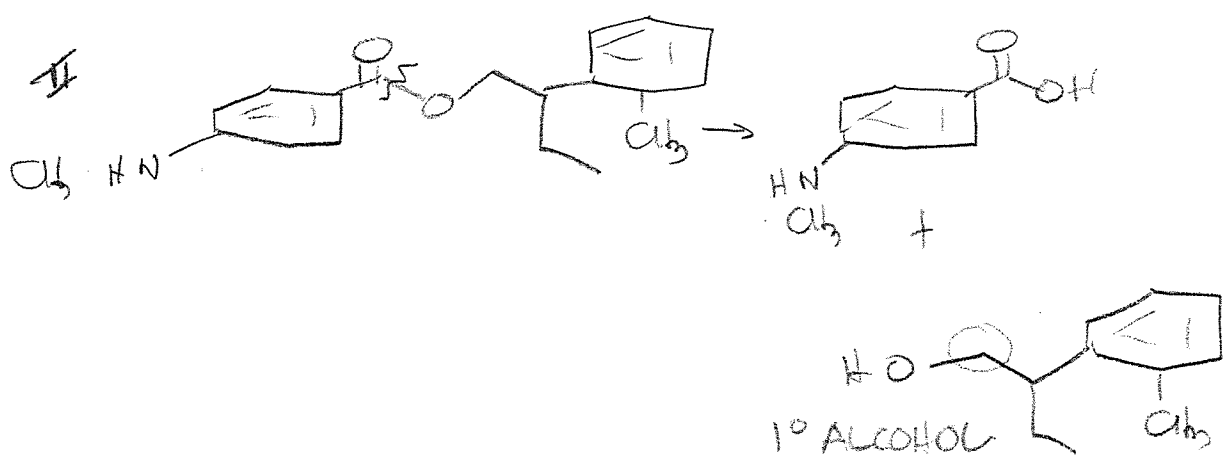
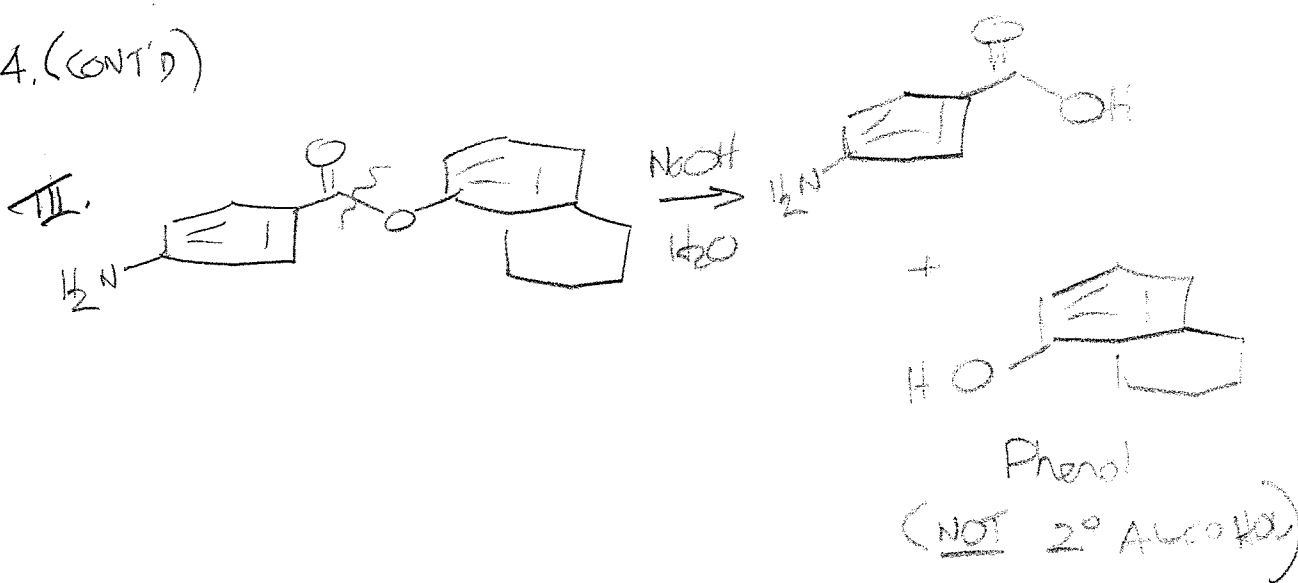


Base catalyzed hydrolysis of benzoate esters occur to form a tetrahedral intermediate (TI) in the rate determining step. The TI is \ominus charged. Substituents on the ring that make the ring \oplus INCREASE the rate of rxn (faster)

Hydrolysis of I, gives a carboxylic acid and 1° alcohol

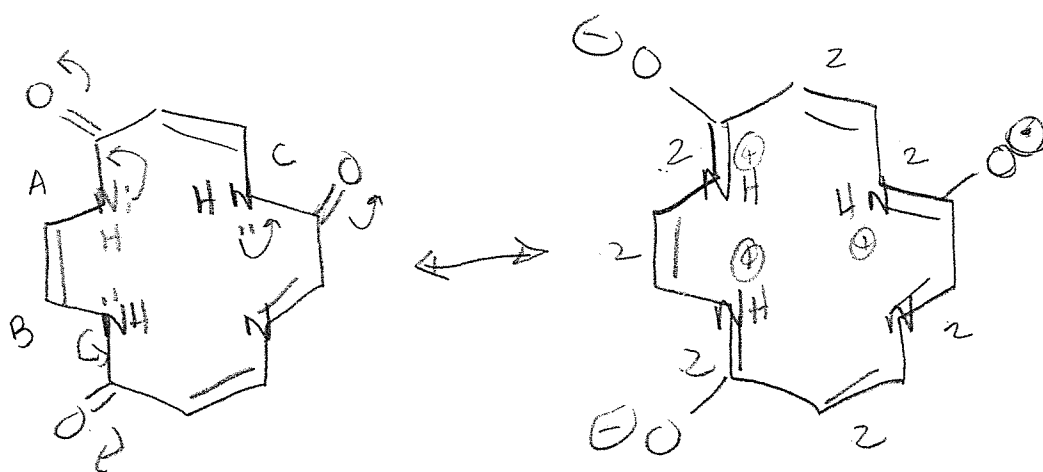


4. (CONT'D)



$\sigma_m = +0.38$
 $\uparrow \oplus$ ring
 FASTER

5.



N: A, B, C delocalize lone pair into carbonyl system to establish PLANAR RING

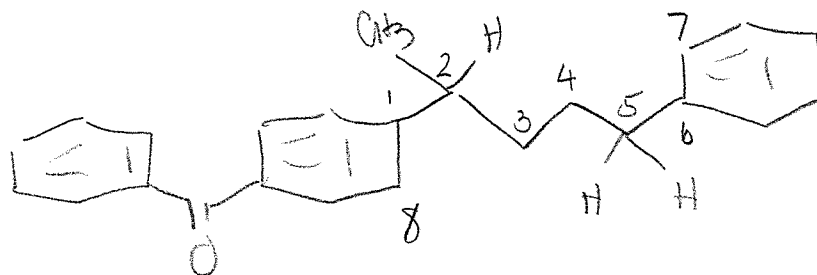
(B)

14 π e⁻ in aromatic system

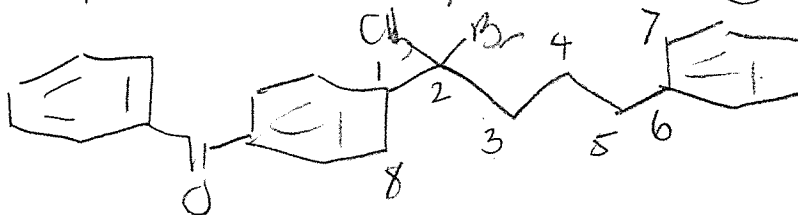
$$4n + 2 = 14$$

$$n = 3$$

6.

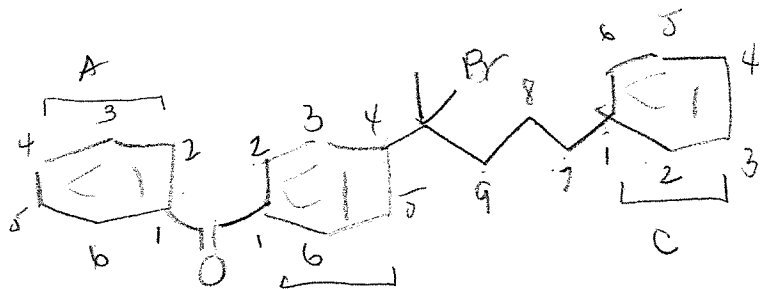


C₂ and C₅ are benzylic carbons w/ at least one hydrogen
 C₂ will react faster w/ NBS, h ν b/c it generates a more stable radical intermediate in the propagation step (rate determining step of the rxn). Product after step 1 is the benzylic bromide (@ C₂) below.



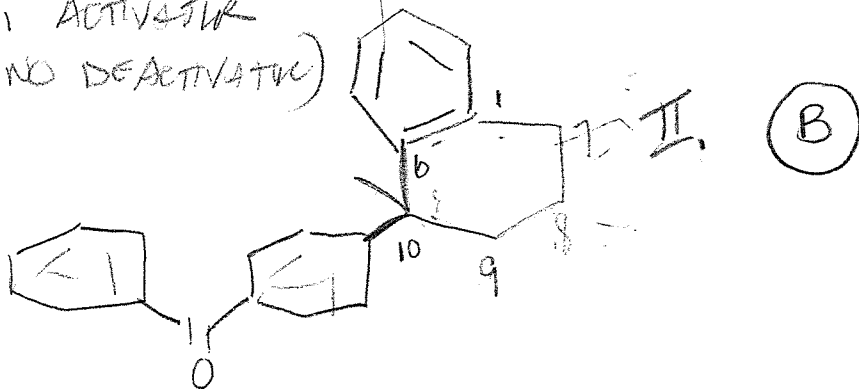
6. (CONT'D)

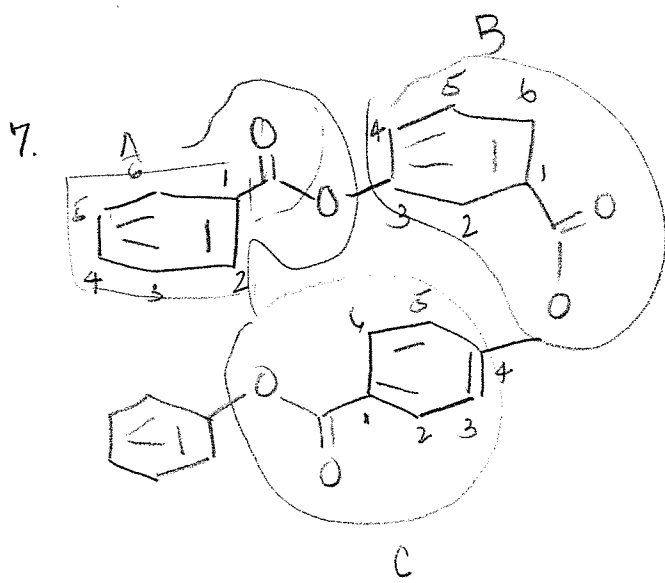
The second step is an INTRAMOLECULAR Friedel Crafts reaction. The rxn will occur on Ring C because it is the most activated.



- A: C1 DEACTIVATOR
- B: C1 DEACTIVATOR
C4 ACTIVATOR
- C: C1 ACTIVATOR
(NO DEACTIVATOR)

Rxn on Ring C occurs ortho to C1 (ie. C6 or C2 = same)

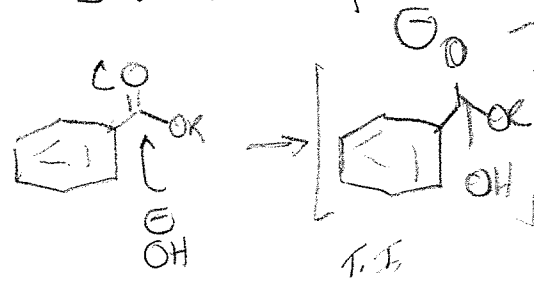




A Ring: No substituents
 B Ring: Acetoxy substituent @ C3
 meta to ester
 $\sigma_m = +0.39$

C Ring: Acetoxy @ C4 para to ester
 $\sigma_p = -0.01$

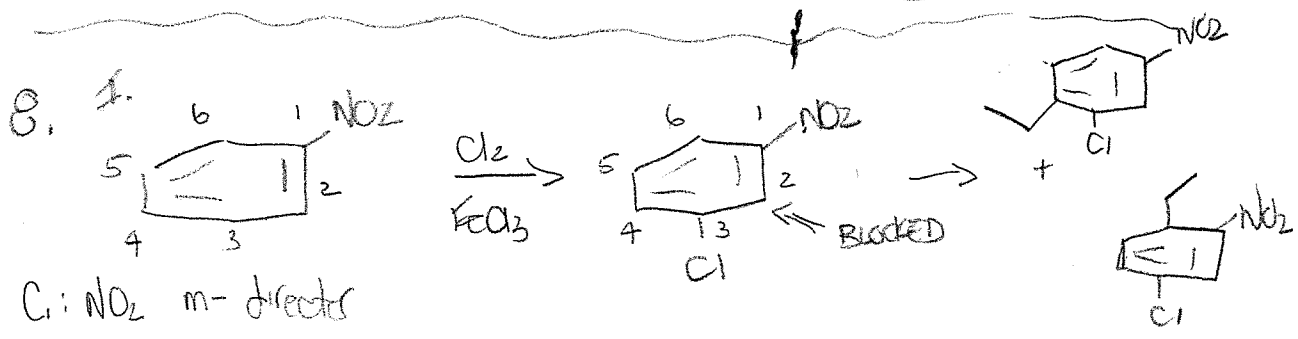
BENZOATE ESTER



The rate determining step of the base catalyzed hydrolysis results in formation of a \ominus tetrahedral intermediate (TI).
 Substituents on the ring that $\uparrow \oplus$ character of ring (i.e. $\oplus \sigma$ value) increase rate of this rxn

B ring MOST \oplus
 Reacts fastest

(A)



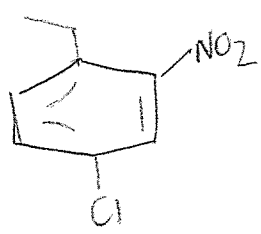
C1: NO₂ m-director

$\sigma_p = +0.78$ C1: NO₂ m-director -Directs to C5

$\sigma_p = +1.23$ C3: Cl o,p-director Directs to C4, C6

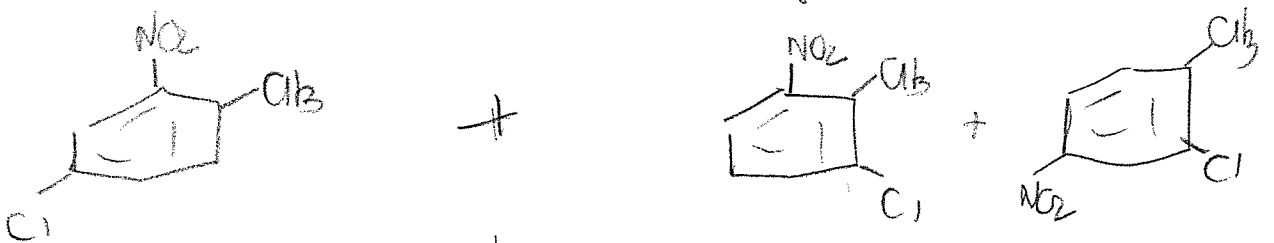
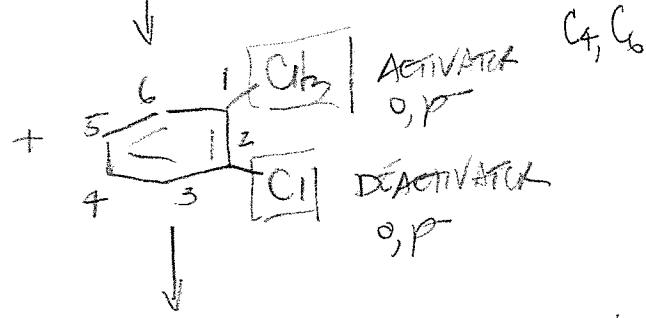
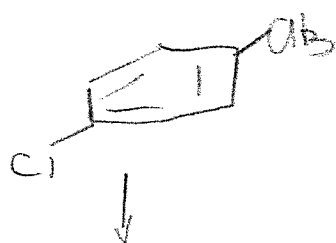
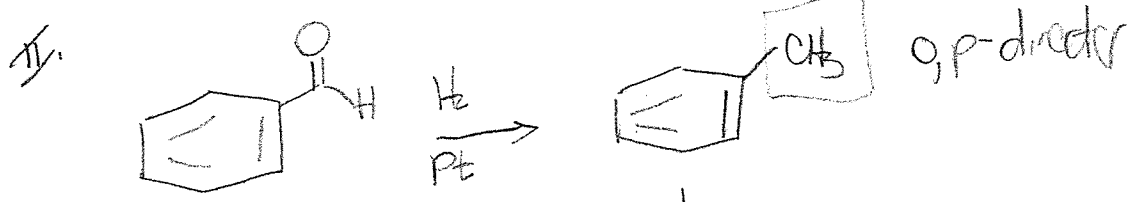
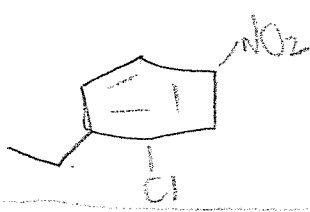
Follows Cl since LEAST DEACTIVATING
 (If NO₂ directs, still does not lead to product)

8. I. (CONT'D)

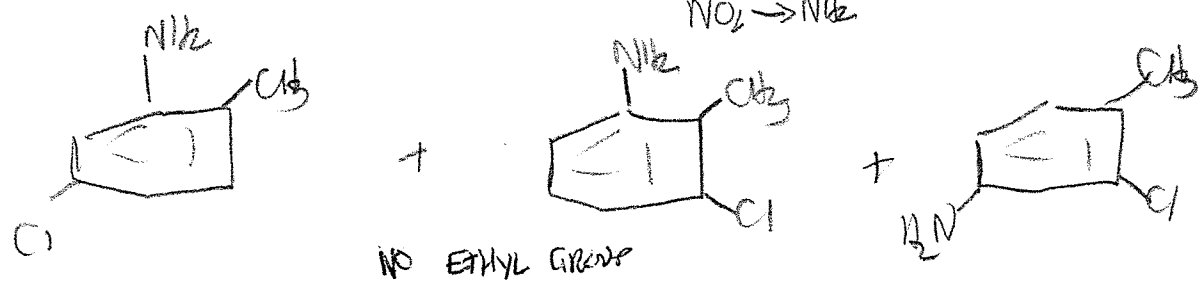


Wolff-Kishner
 \xrightarrow{KOH}
 H_2NNH_2
 NO RXN

NOT 1-amino-2-chloro-4-ethylbenzene
 benzene



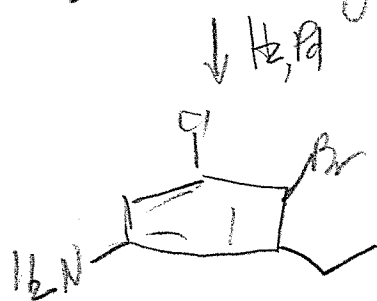
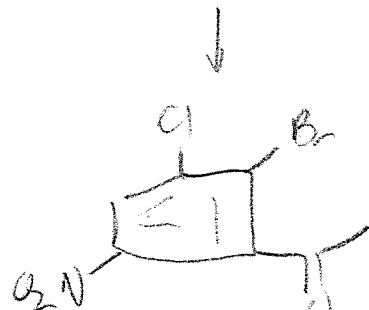
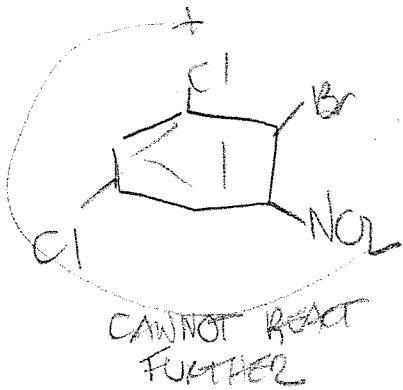
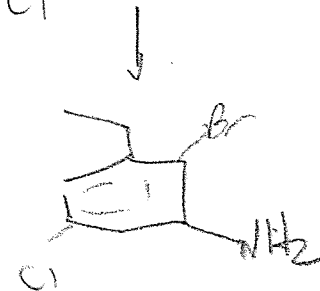
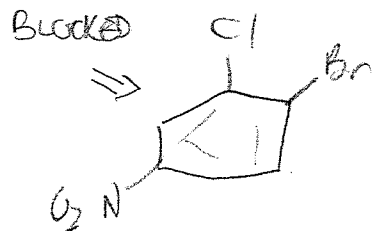
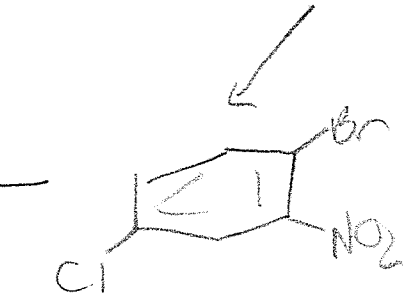
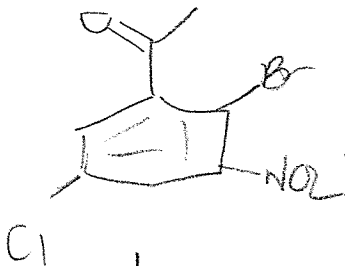
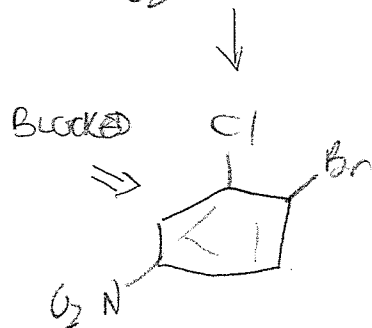
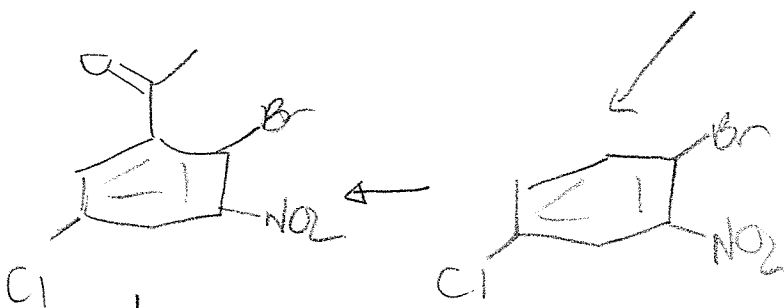
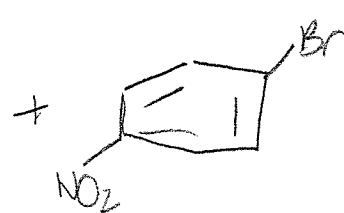
$\downarrow H_2, Pd$ (Reduces NO₂ \rightarrow NH₂)



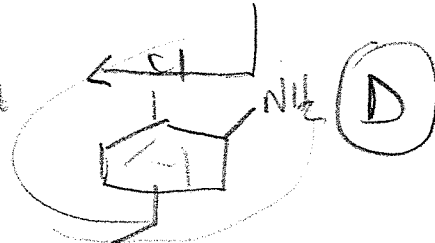
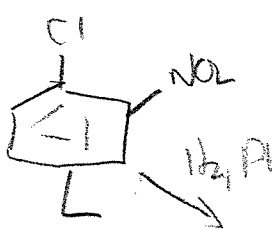
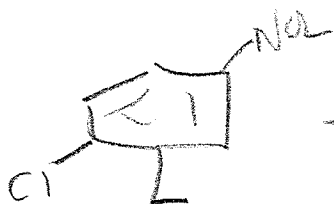
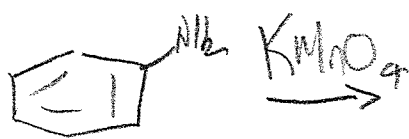
NO ETHYL GROUPS

8. (CONT'D) \downarrow o,p-director

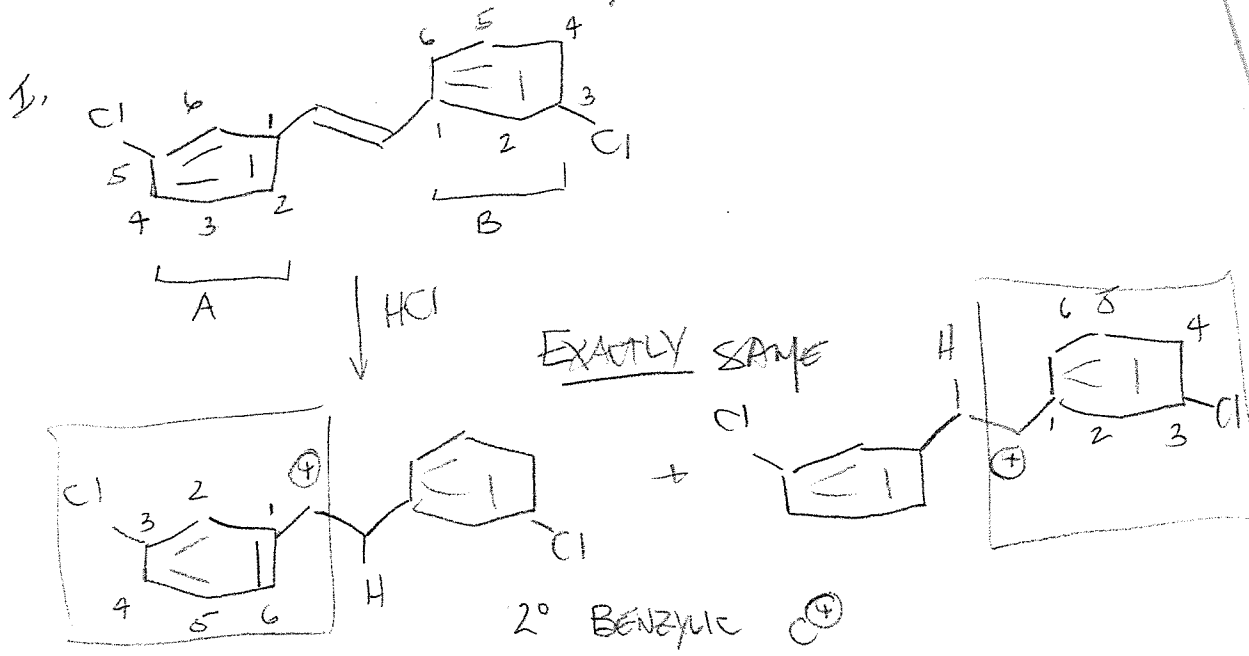
III.



IV



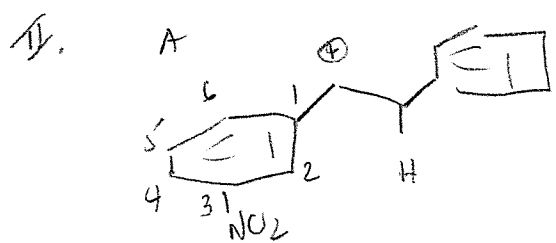
9. Electrophilic addition of styrene



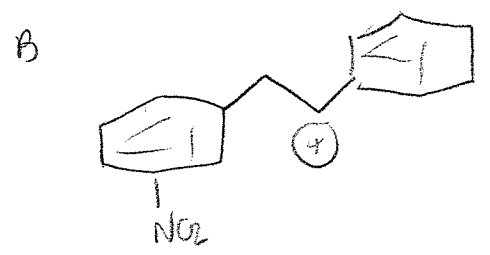
Cl @ C₃ $\sigma_m = +0.31$

Cl @ C₃ $\sigma_m = +0.31$

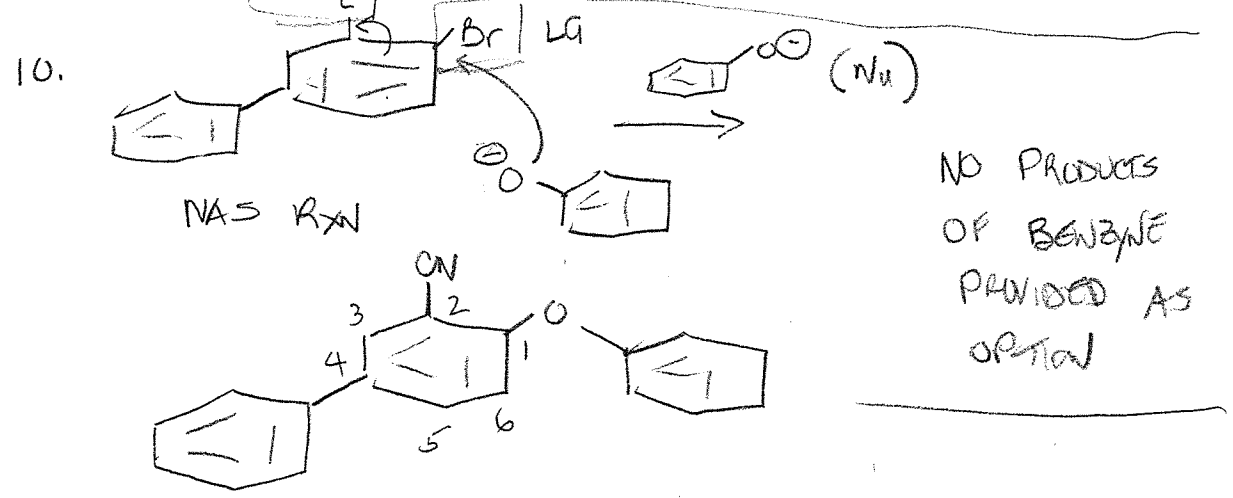
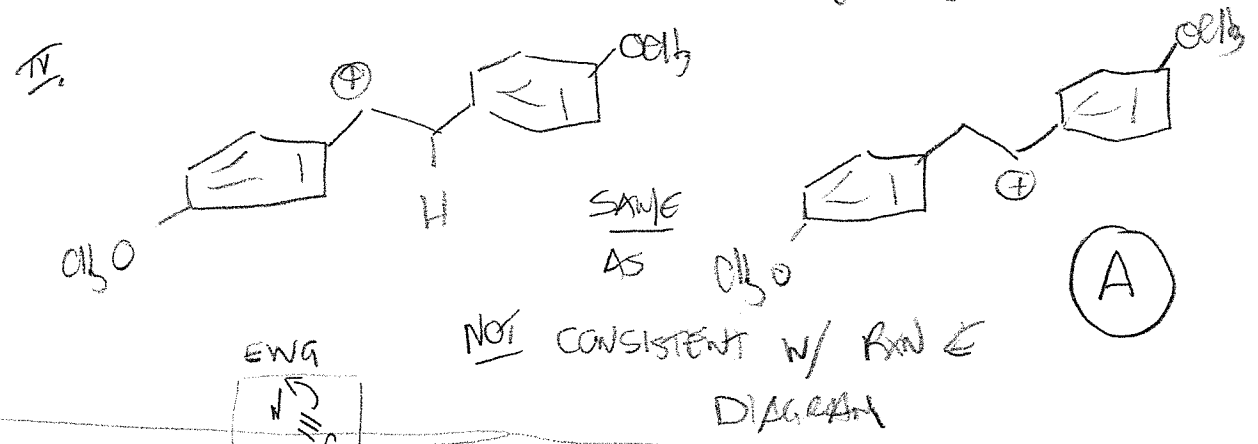
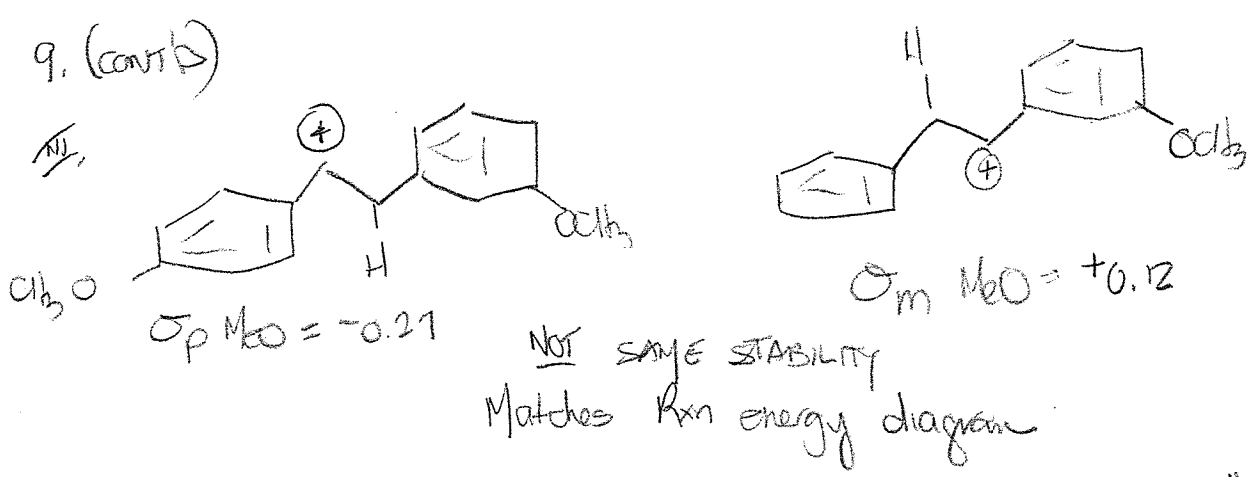
SAME EXACT STABILITY
DOES NOT CORRESPOND TO RXN E DIAGRAM
WHICH SHOWS 2 C⁺ intermediate of different
stability



σ_m NITRO = +0.71
LESS STABLE



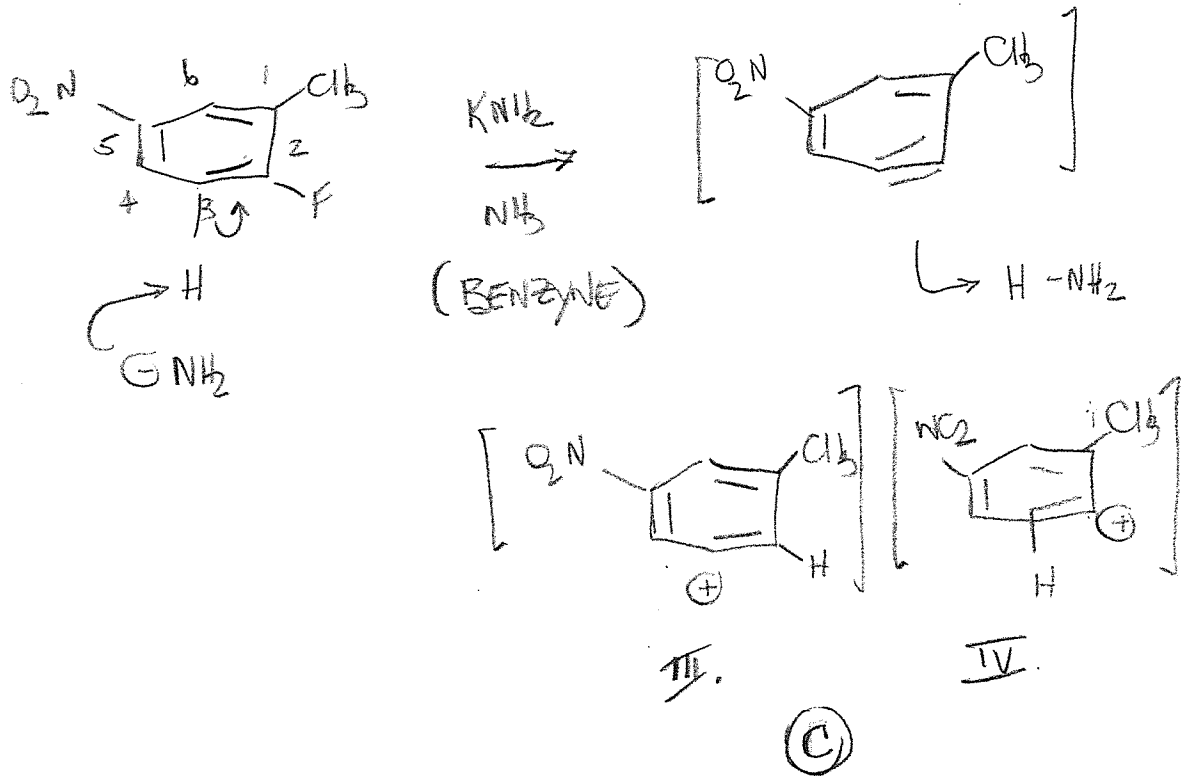
Matches Rxn E Diagram



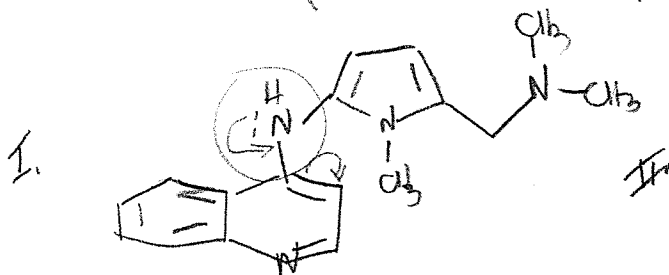
2-cyano-1-phenoxy-4-phenylbenzene

I. (A)

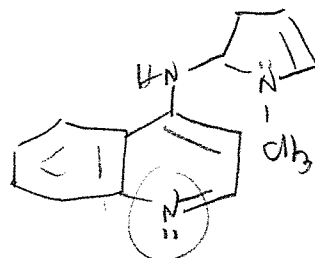
11. 2-FLUORO-5-NITROBENZENE



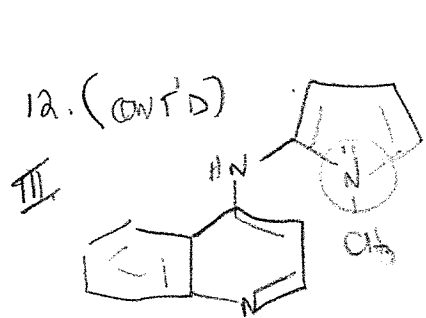
12. STRONGEST BASE: N lone pair not involved in resonance or aromatic ring
 WEAKEST BASE: N lone pair part of AROMATIC RING.



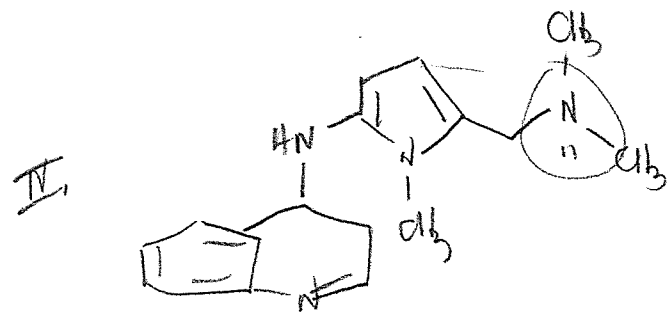
Resonance, NOT involved in aromatic system



Lone pair NOT used for aromaticity of ring. Available to accept proton



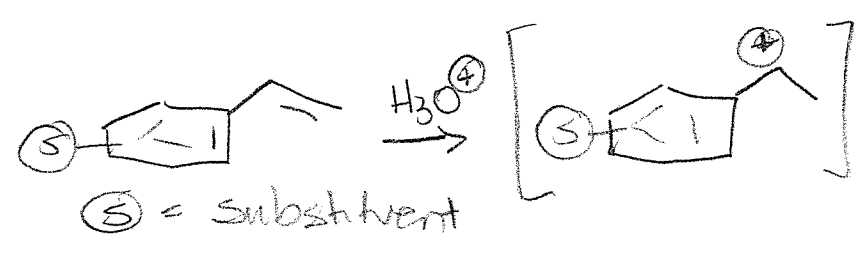
Lone pair part
of aromatic system
NOT available to
accept proton



NO RESONANCE
NO AROMATICITY
Same as II

$$IV = II > I > III \quad (A)$$

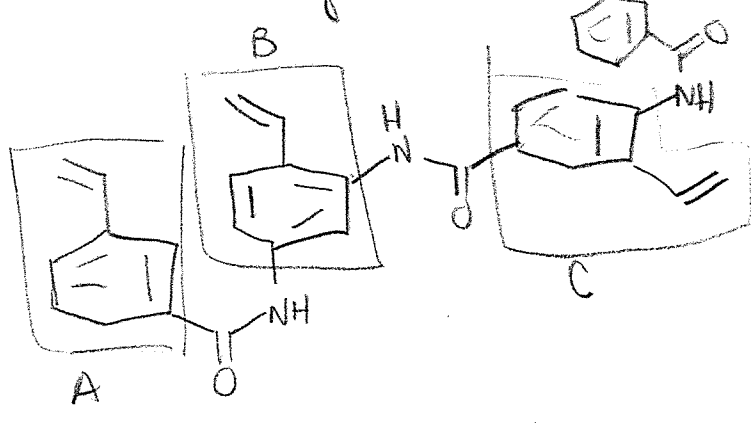
13. Electrophilic addition of styrene



CARBICATION
FORMS IN
RATE DETERMINING
STEP

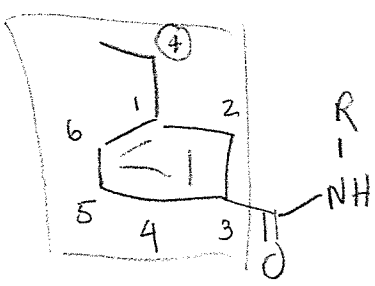
$S \uparrow \oplus$ of ring \Rightarrow Destabilizes \oplus
 $S \uparrow \ominus$ of ring \Rightarrow Stabilizes \oplus

SLOWER RXN
FASTER RXN



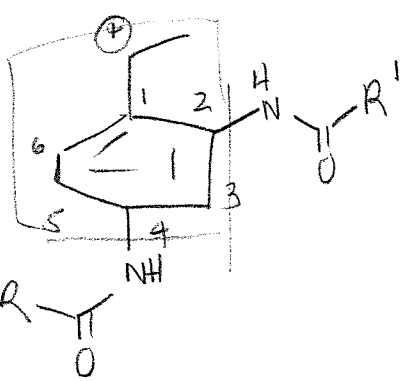
B. (CONT'D)

A RING.



C3 ACETYL $\sigma_m = +0.38$

B RING

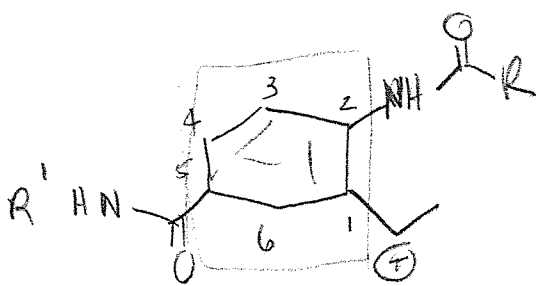


C2 ACETAMIDO $\sigma_p = -0.02$

C4 ACETAMIDO $\sigma_p = \frac{-0.02}{0.04}$

(E)

C RING

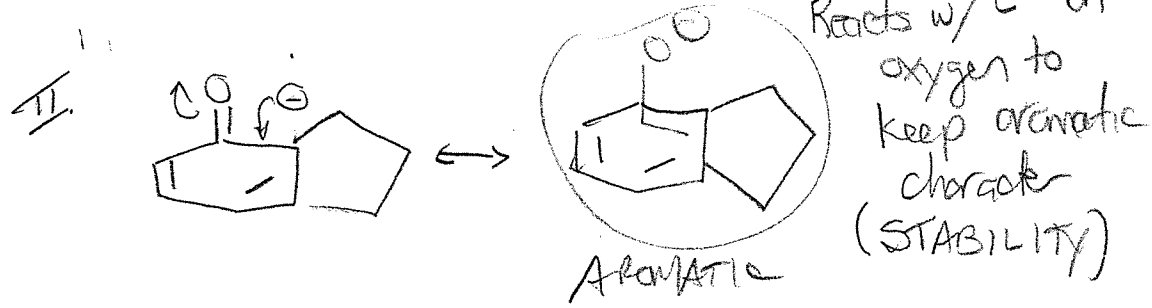
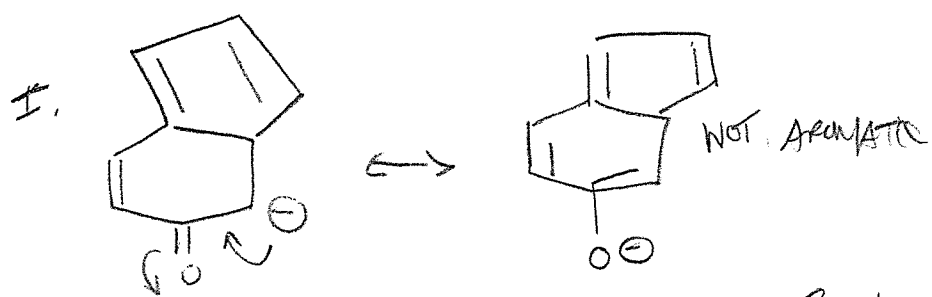


C2 ACETAMIDO $\sigma_p = -0.02$

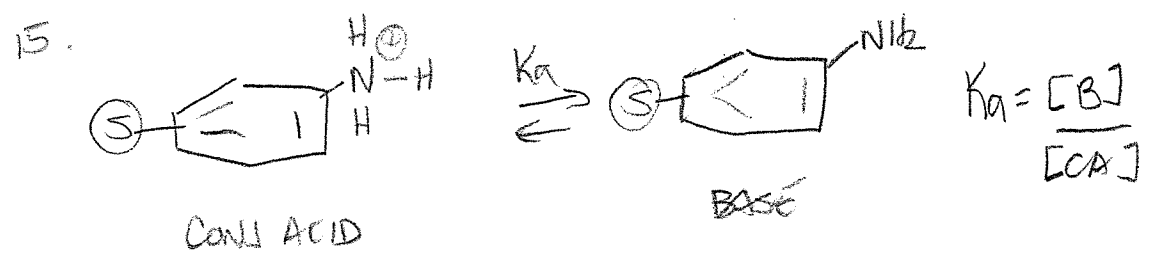
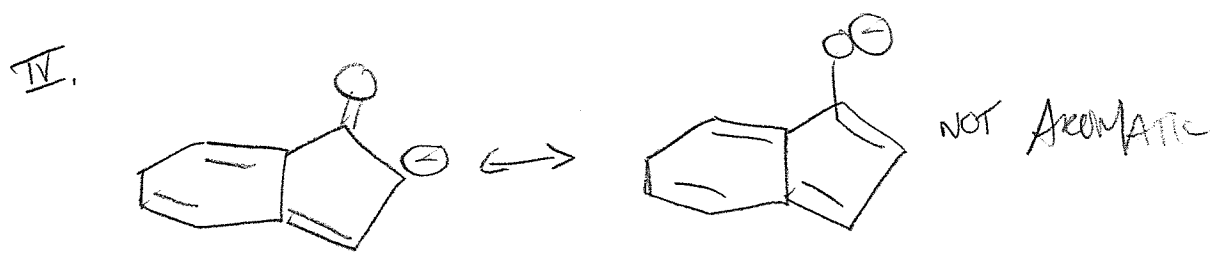
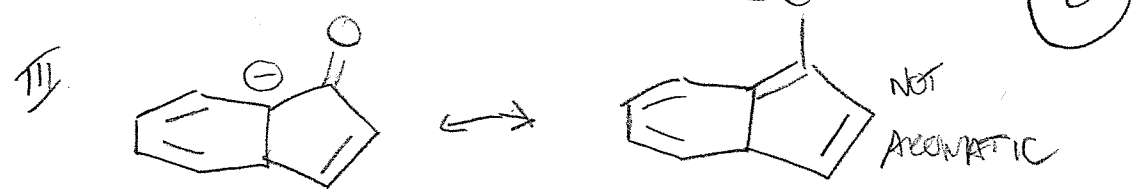
C5 ACETYL $\sigma_m = +0.38$

+0.36

14.



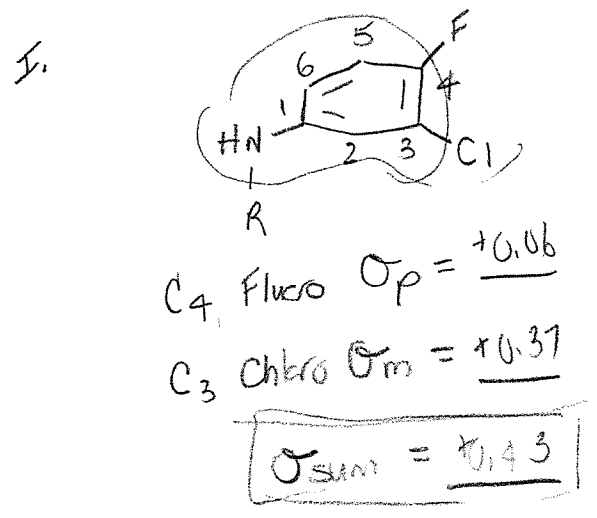
14. (CONT'D)



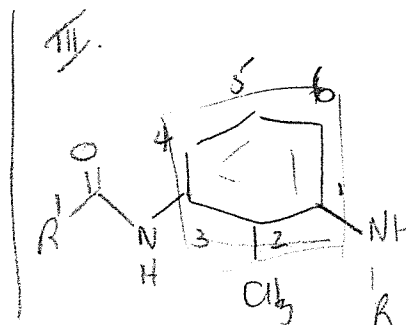
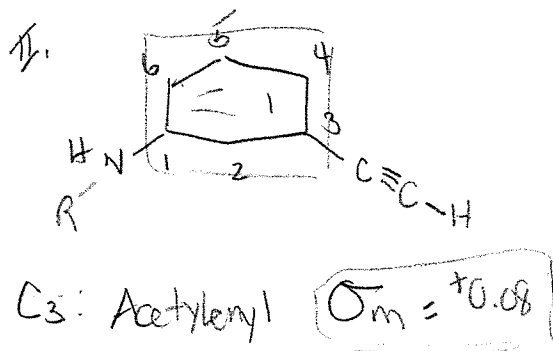
Ⓢ = substituent

Ⓢ ↑ ⊖ ring (⊖ σ value)
 STABILIZE CA
 ↑ [CA] ↓ K_a ↑ pK_a ↓ pK_b
 STRONGER BASE

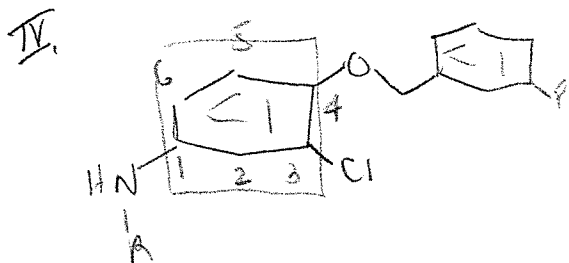
Ⓢ ↑ ⊕ ring (⊕ σ value)
 DESTABILIZE CA
 ↓ [CA] ↑ K_a ↓ pK_a ↑ pK_b
 WEAKER BASE



15. (cont'd)



$\sigma_{sum} = +0.04$

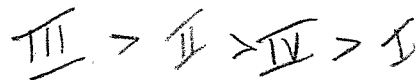


C₃ Chloro Cl $\sigma_m^+ = 0.37$

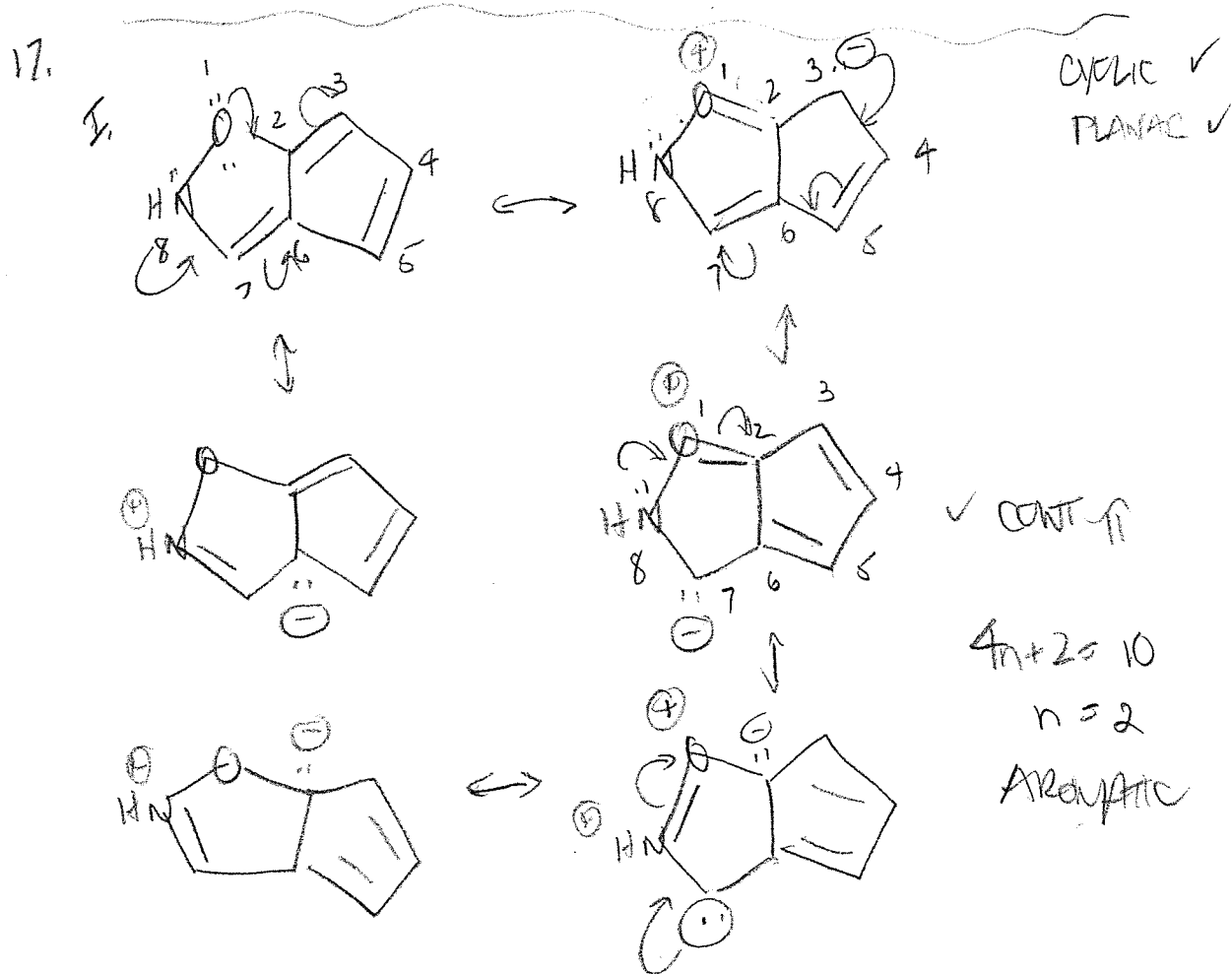
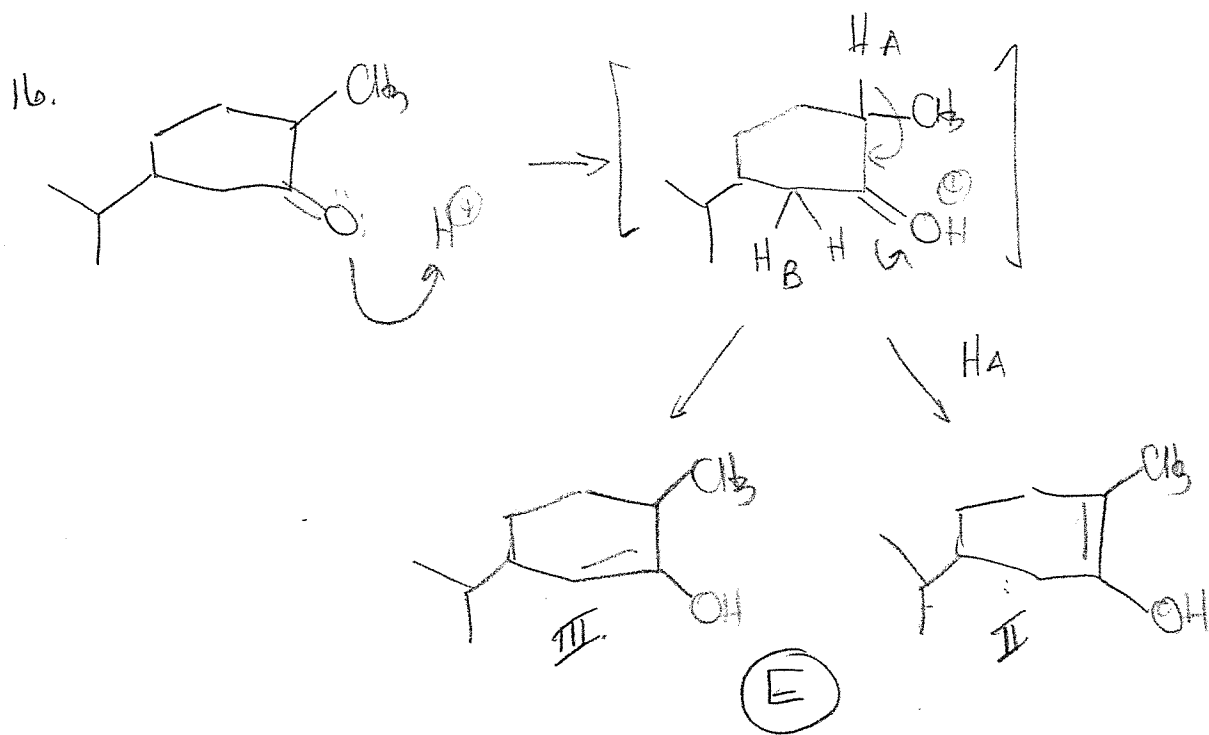
C₄ Methoxy OR $\sigma_p = -0.27$

$\sigma_{sum} = +0.10$

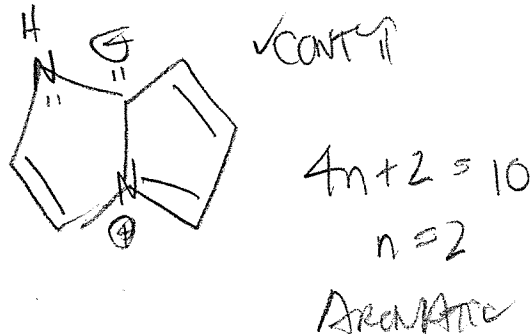
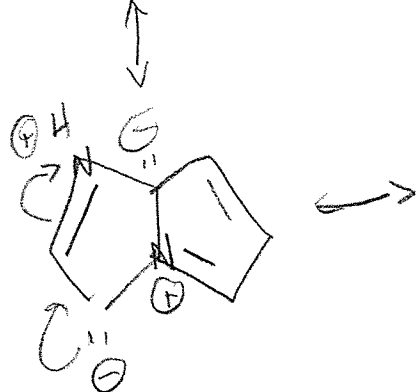
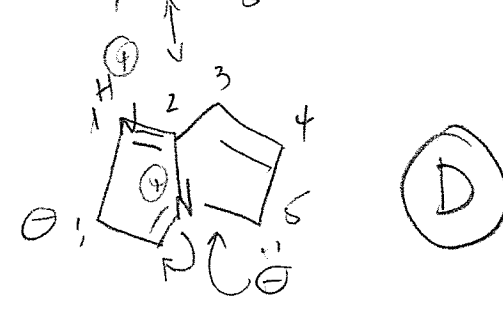
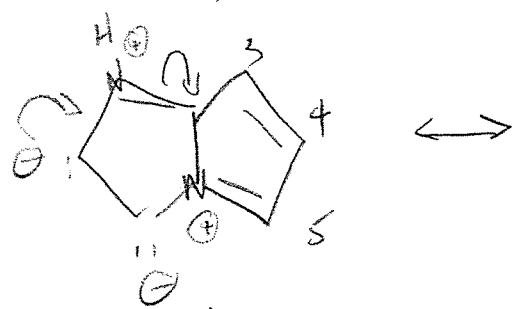
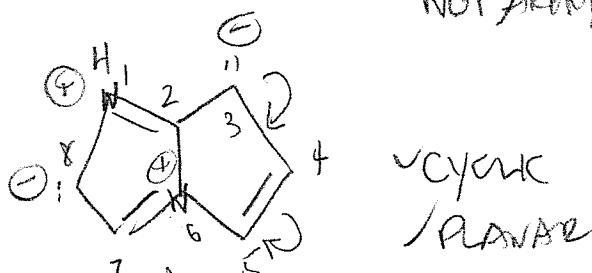
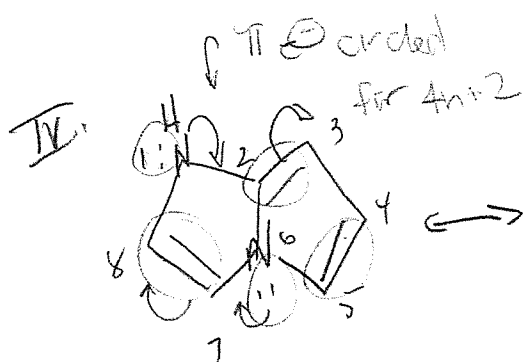
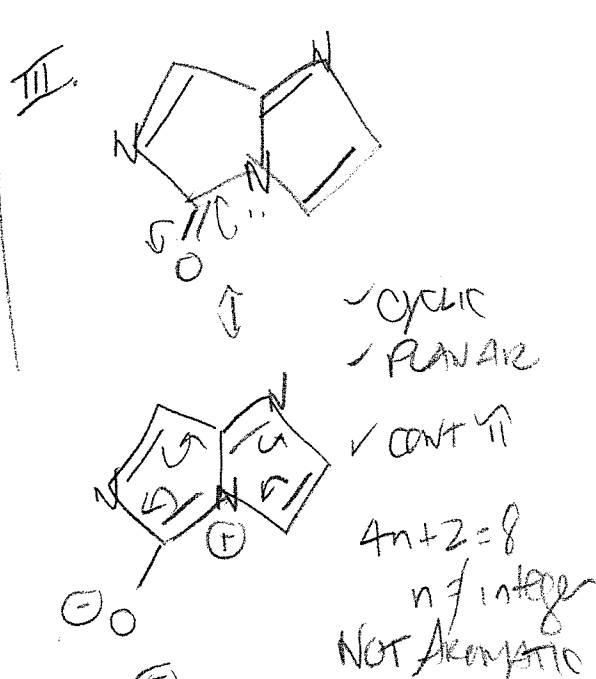
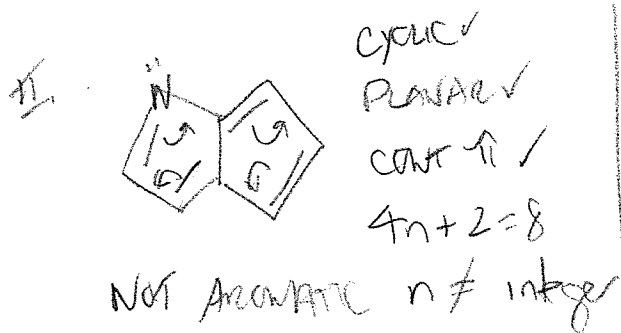
Most ⊕ ring: Lowest pKa
 LEAST ⊕ ring: Highest pKa



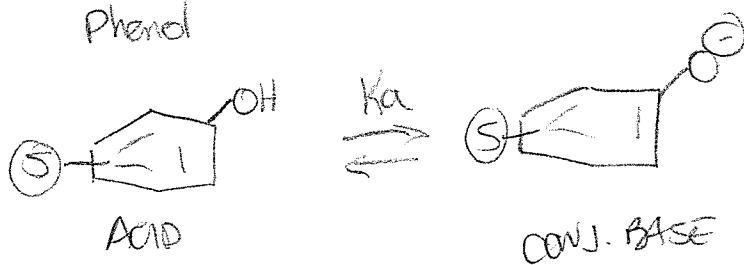
(B)



12. (cont'd)



18. Phenol



(S) = substituent

LOWEST pKa

(S) ↑ ⊕ ring (⊕ σ value)

STABILIZE CB

↑ [CB] ↑ Ka ↓ pKa

STRONGER ACID

(A)

HIGHEST pKa

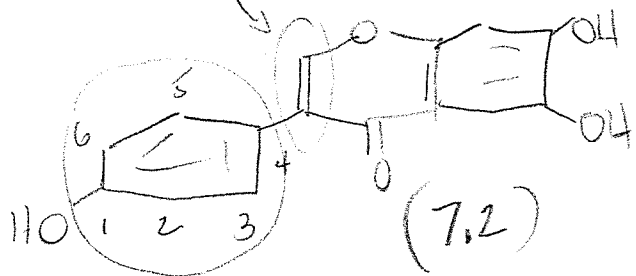
(S) ↑ ⊖ ring (⊖ σ value)

DESTABILIZE CB

↓ [CB] ↓ Ka ↑ pKa

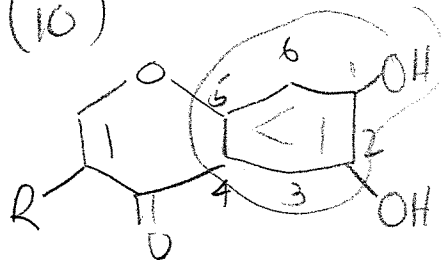
WEAKER ACID

A



C4, ALKENYL $\sigma_p = -0.02$

B (10)



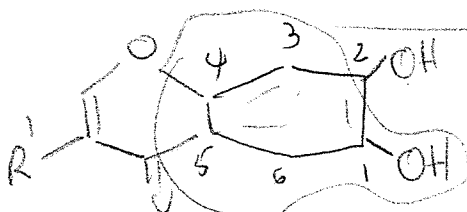
C2 Hydroxy $\sigma_p = -0.37$

C4 Acetyl $\sigma_p = +0.5$

C5 OCH₃ $\sigma_m = +0.12$

$\sigma_{sum} = -0.20$

C



HIGHEST (13,1)

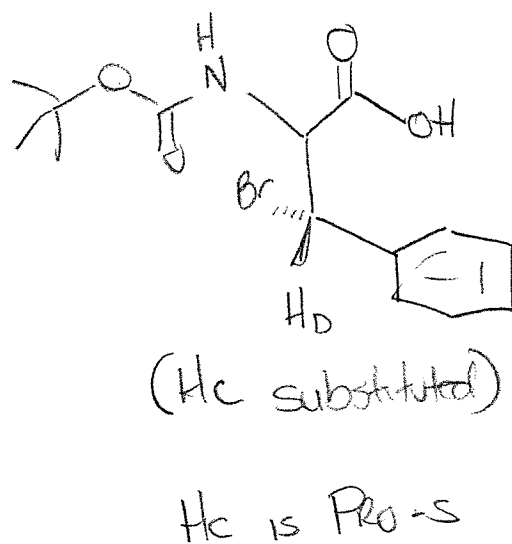
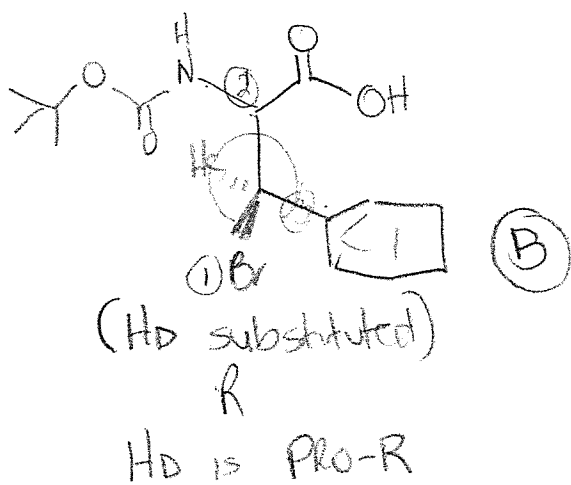
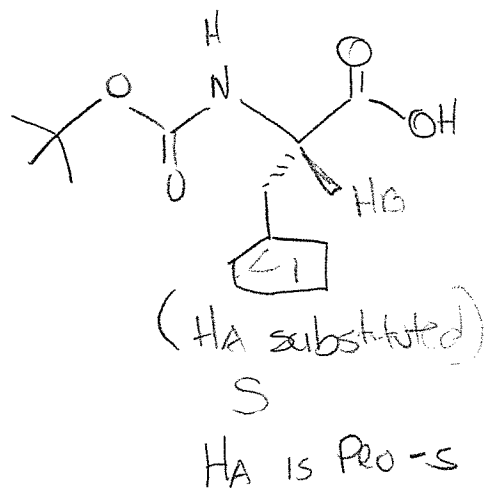
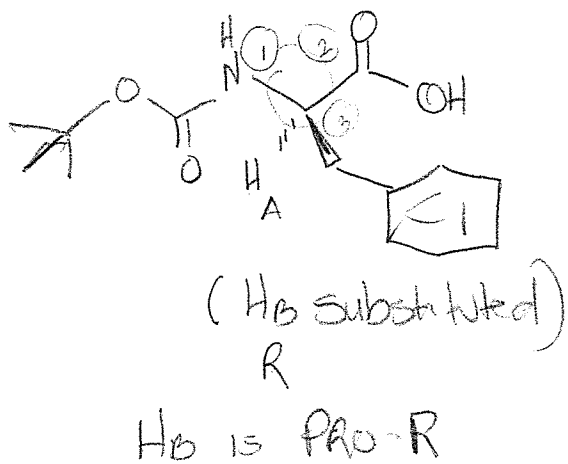
C2 Hydroxy $\sigma_p = -0.37$

C4 OCH₃ $\sigma_p = -0.27$

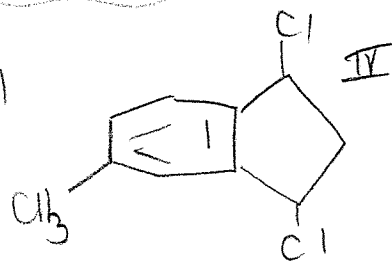
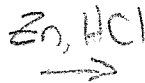
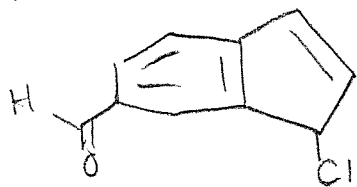
C5 Acetyl $\sigma_m = +0.38$

$\sigma_{sum} = -0.26$

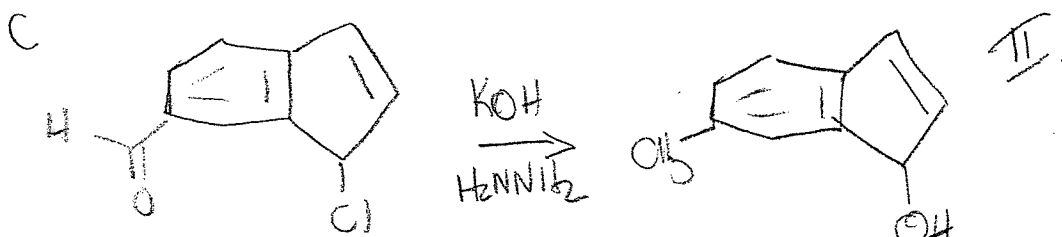
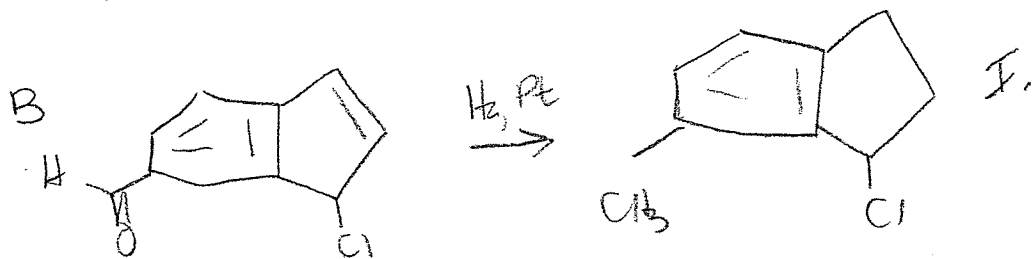
19.



26. A:



20. (cont'd)

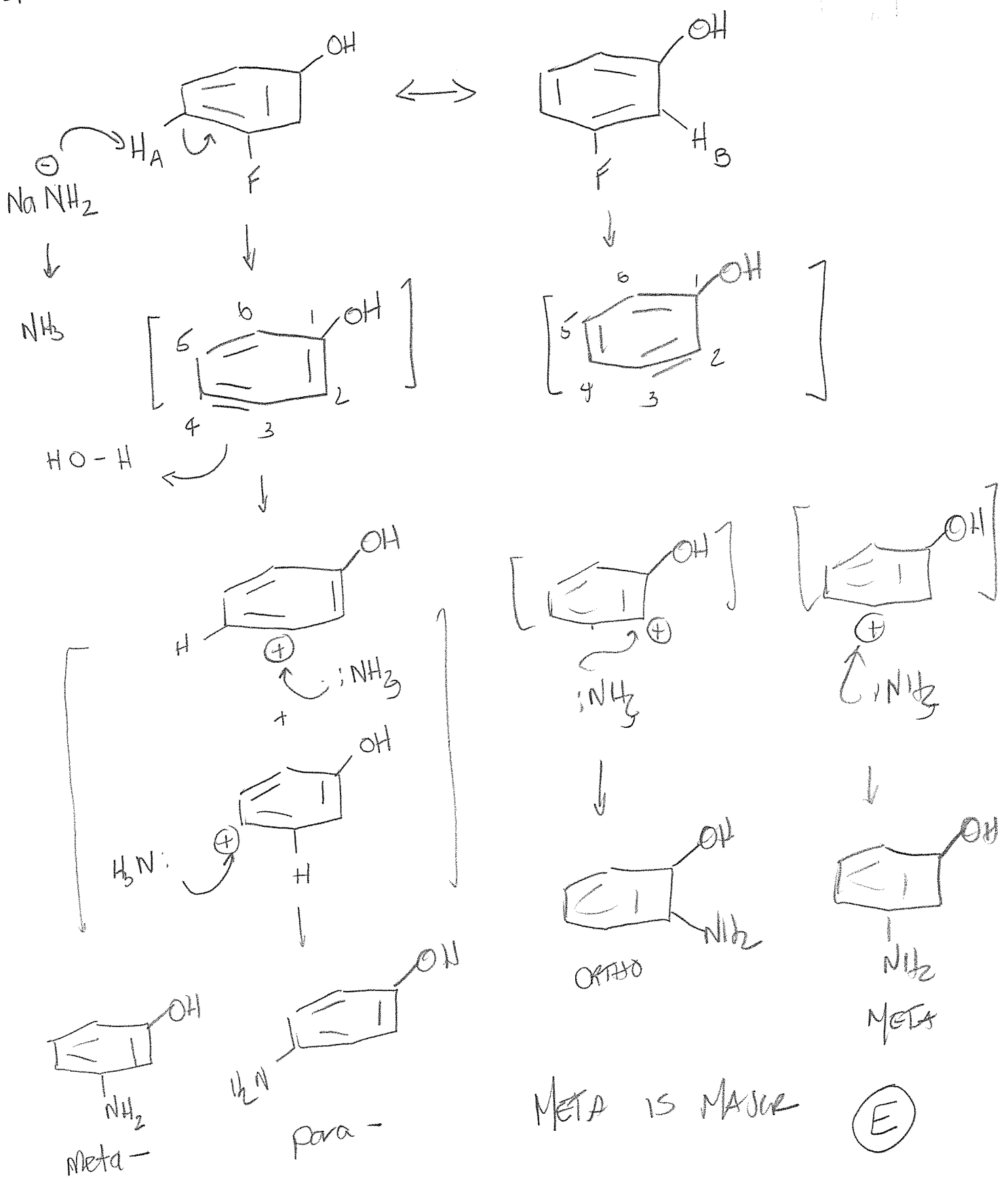


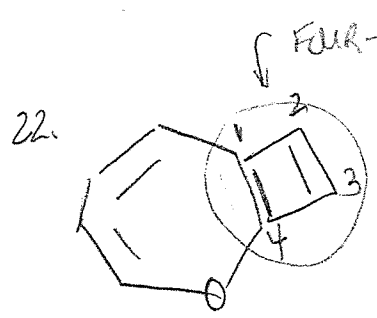
A = IV B = I C = II

C

21.

21



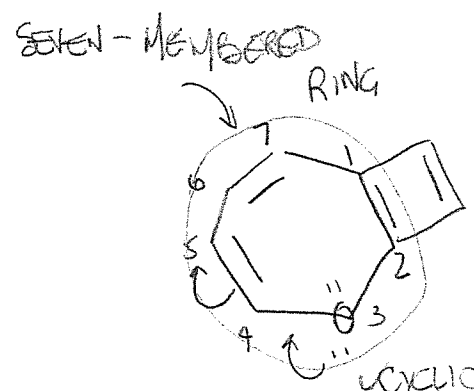


FOUR-MEMBERED RING
 ✓ CYCLIC
 ✓ PLANAR
 ✓ CONT π

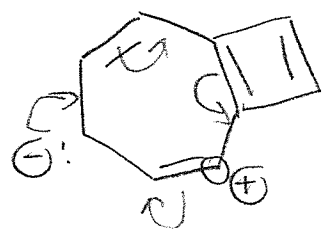
$4n+2=4$
 $n \neq \text{integer}$

I. FALSE

IV. TRUE

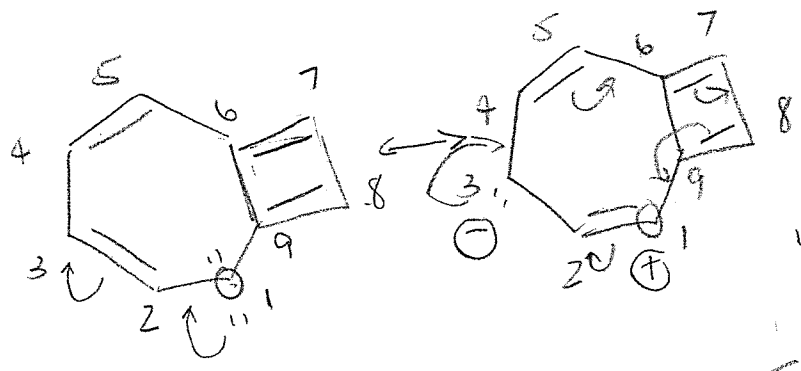


✓ CYCLIC
 - PLANAR
 ✓ CONT π
 $4n+2=8$
 $n \neq \text{integer}$



II. FALSE

(E)



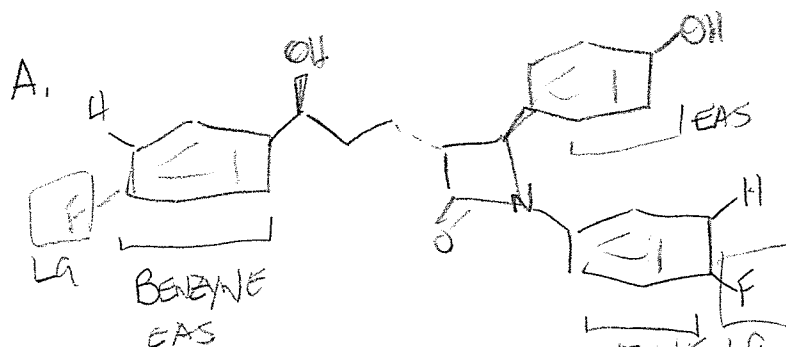
✓ CYCLIC
 ✓ PLANAR
 ✓ CONT π
 $4n+2=10$
 $n=2$

AROMATIC
 III. TRUE

23. EAS: must have "open" carbon bonded to H on ring and NOT flanked by substituents on both sides

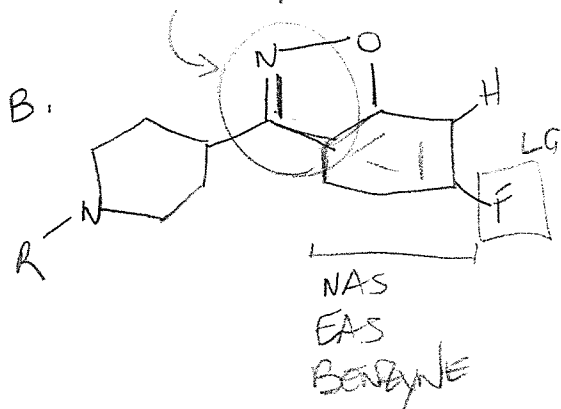
NAS: must have LG and EWG by resonance ortho or para to LG

BenzylNE: must have LG and ortho H

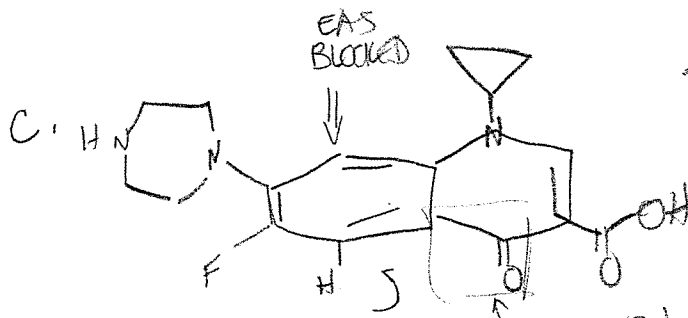


I & III

EWG by resonance



I, II, & III

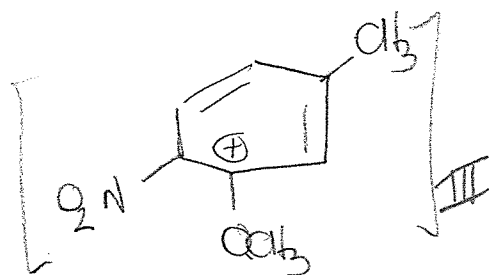
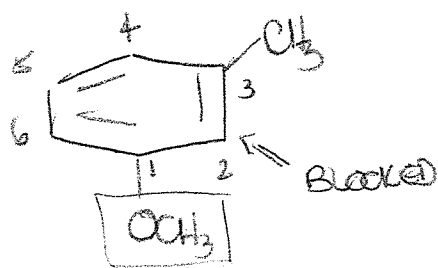


III only

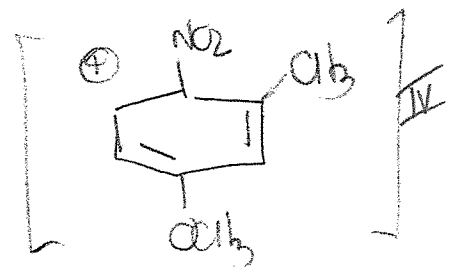
EAS BLOCKED BUT BENZYLNE OKAY
EWG by resonance but META to LG



24.

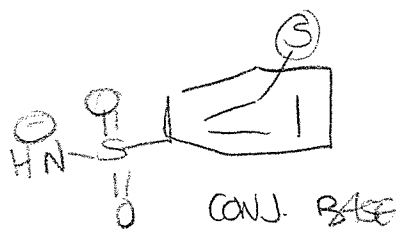
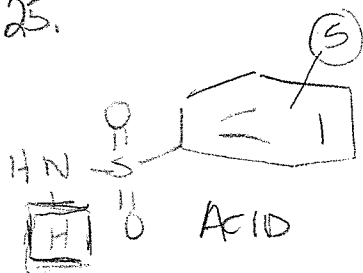


C. OCH_3 ACTIVATOR ($\sigma_p = -0.27$)
 o,p-director STRONGER ACTIVATOR
 C_4, C_6



$\text{C}_3 \text{CH}_3$ ACTIVATOR ($\sigma_p = -0.17$)
 o,p-director
 C_4, C_6

25.



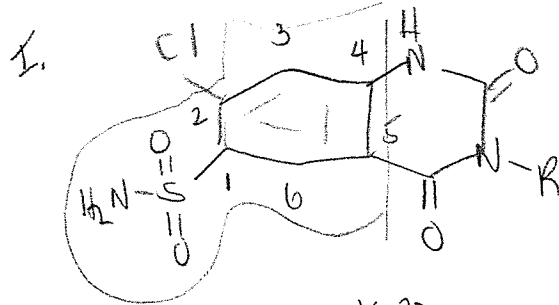
$$K_a = \frac{[\text{CB}]}{[\text{A}]}$$

(S) = substituent

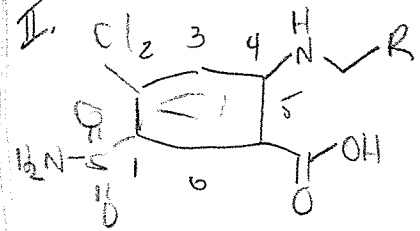
(S) \uparrow \oplus ring ($\oplus \sigma$ values)
 STABILIZE CB \uparrow [CB]
 $\uparrow K_a \downarrow pK_a$ STRONGER ACID

(S) \uparrow \ominus ring ($\ominus \sigma$ values)
 DESTABILIZE CB \downarrow [CB]
 $\downarrow K_a \uparrow pK_a$ WEAKER ACID

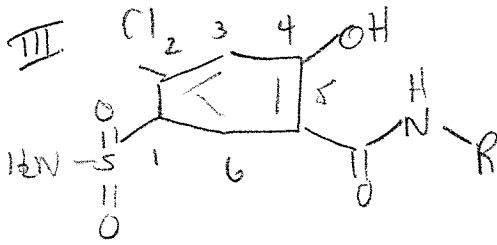
25. (CONT'D)



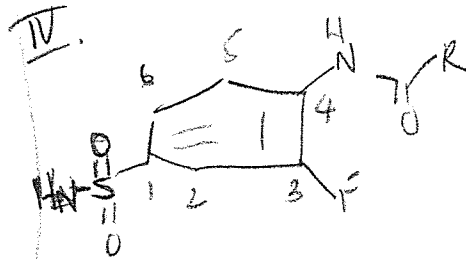
C₂ CHLORO $\sigma_p = +0.23$
 C₄ ACETAMIDO $\sigma_p = -0.02$
 C₅ ACETYL $\sigma_m = +0.38$
+0.59



C₂: CHLORO $\sigma_p = +0.23$
 C₄: AMINO $\sigma_p = -0.66$
 C₅: ACETYL $\sigma_m = \frac{+0.38}{2.3}$
-0.05



C₂ CHLORO $\sigma_p = +0.23$
 C₄ HYDROXY $\sigma_p = -0.37$
 C₅ ACETYL $\sigma_m = +0.38$
+0.24

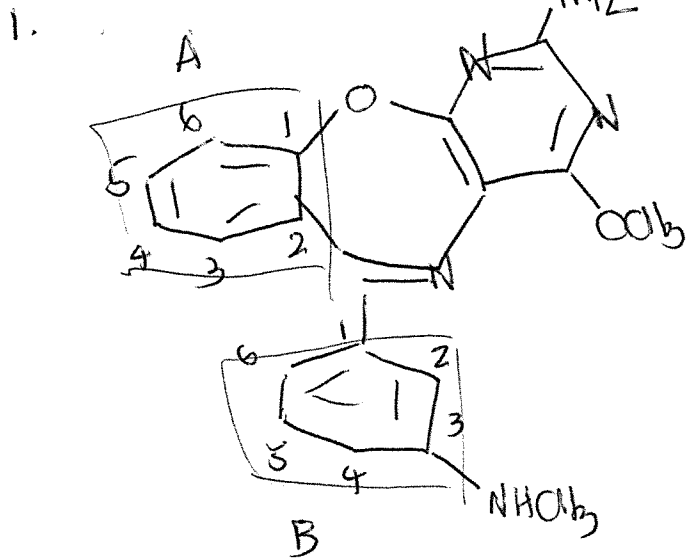


C₃ FLUORO $\sigma_m = +0.34$
 C₄ ACETAMIDO $\sigma_p = -0.02$
+0.32

Most \ominus strongest acid

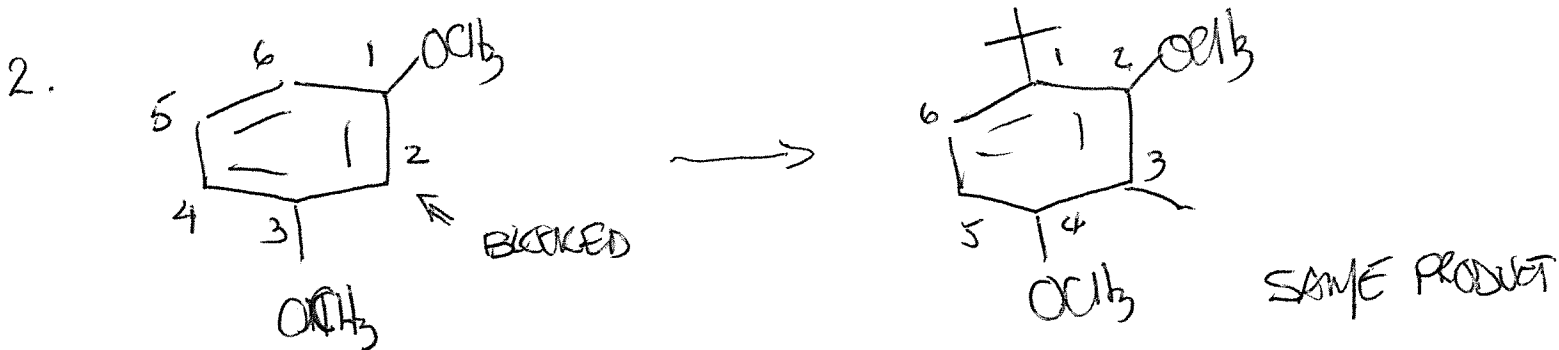
I > IV > III > II

(A)



RING A:	C ₁	OC=CH ₃	ACETYL	$\sigma_p = -0.01$
	C ₂	C≡N	CYANO	$\sigma_p = +0.66$
				$+0.65$
RING B	C ₁	C≡N	CYANO	$\sigma_p = +0.66$
	C ₃	NHCOCH ₃	AMIDO	$\sigma_p = -0.66$
				$\sigma_{sum} = 0$

MORE \ominus / LESS \oplus
 MOST ACTIVATED
 OCCURS AT C₄, C₆
 ON RING B III + IV
 (C)



C₁ OMe C₄, C₆
 C₃ OMe C₄ C₆

