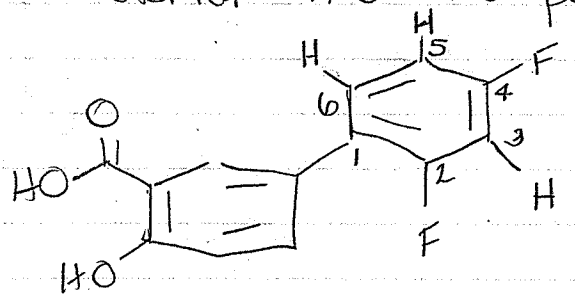
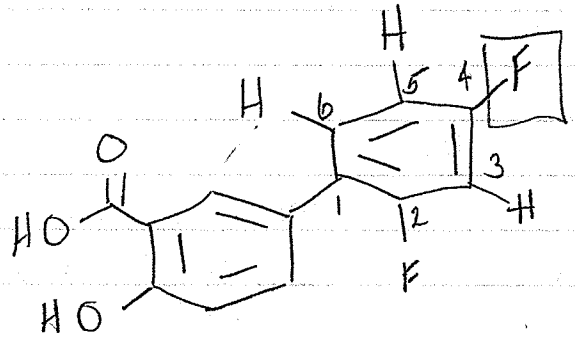
S2015
EXAM 3
SOLUTIONS

1. The reaction is a BENZYNE mechanism. The starting material has two possible leaving groups (F) at C_2 and C_4

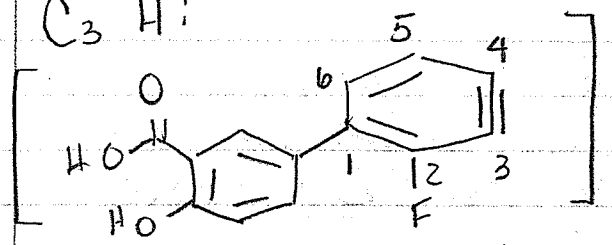


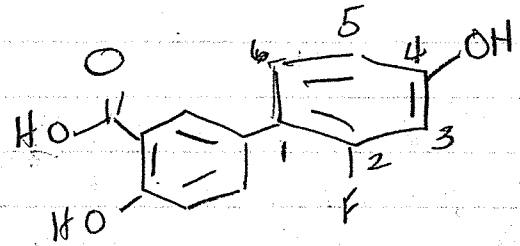
C F @ C_4 :



Benzyne can form from F and H @ C_3 or H @ C_5

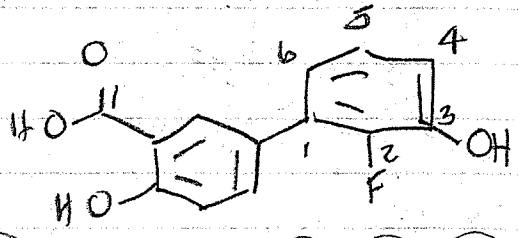
C_3 H:





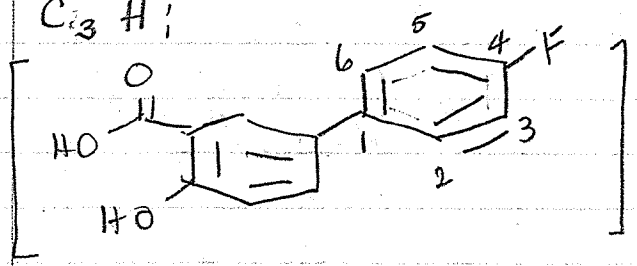
I.

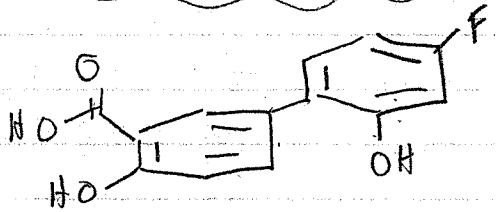
+



II.

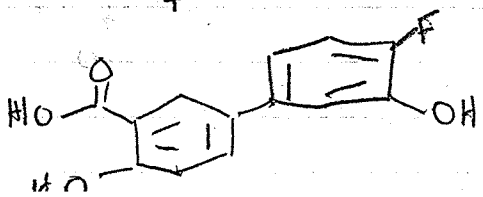
C_3 H:



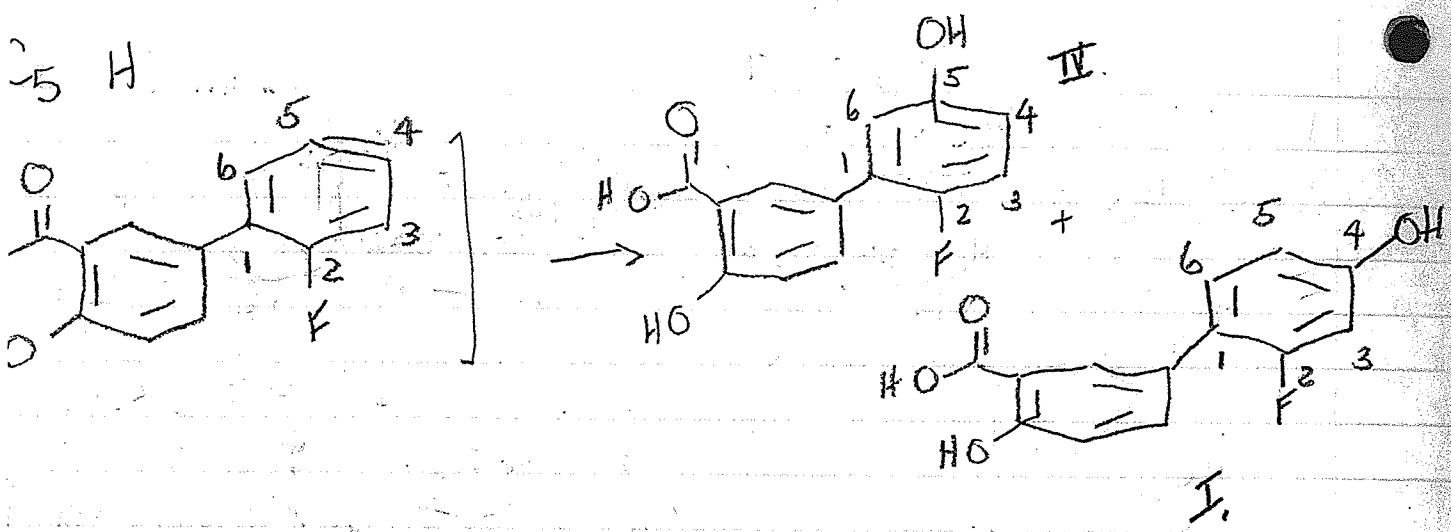


III.

+

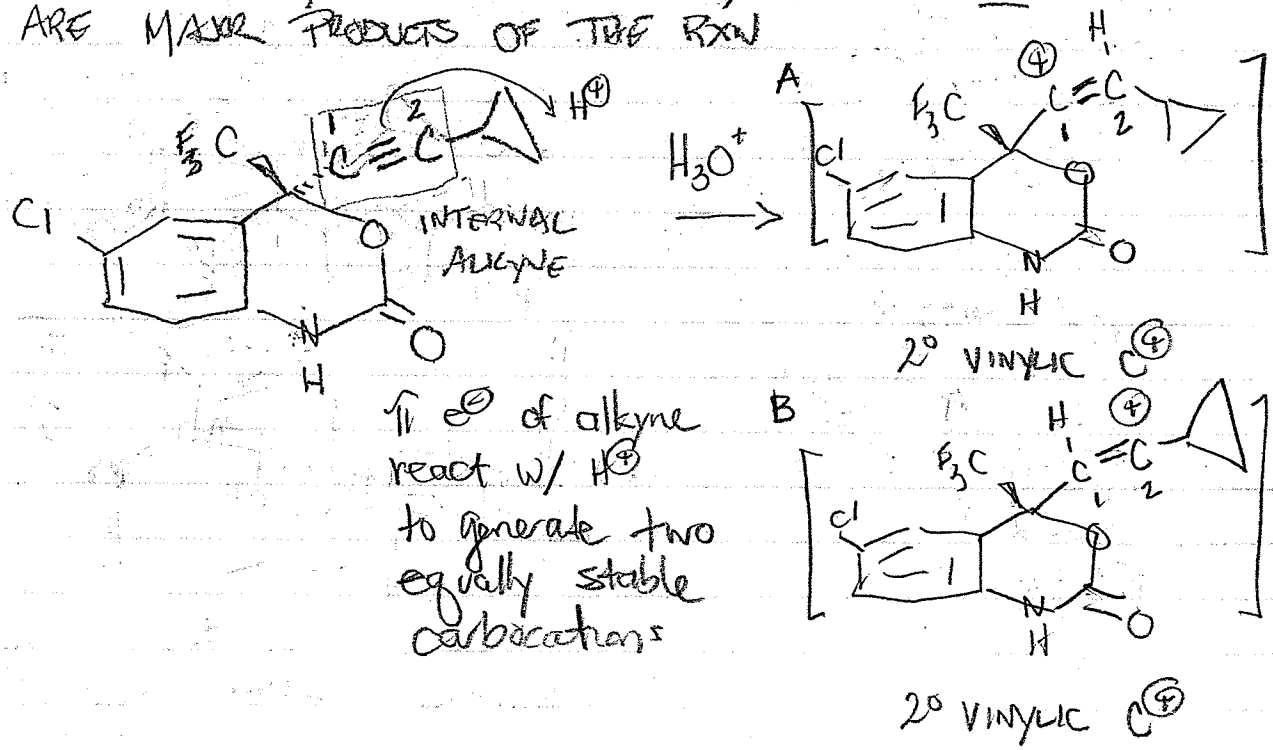


IV.



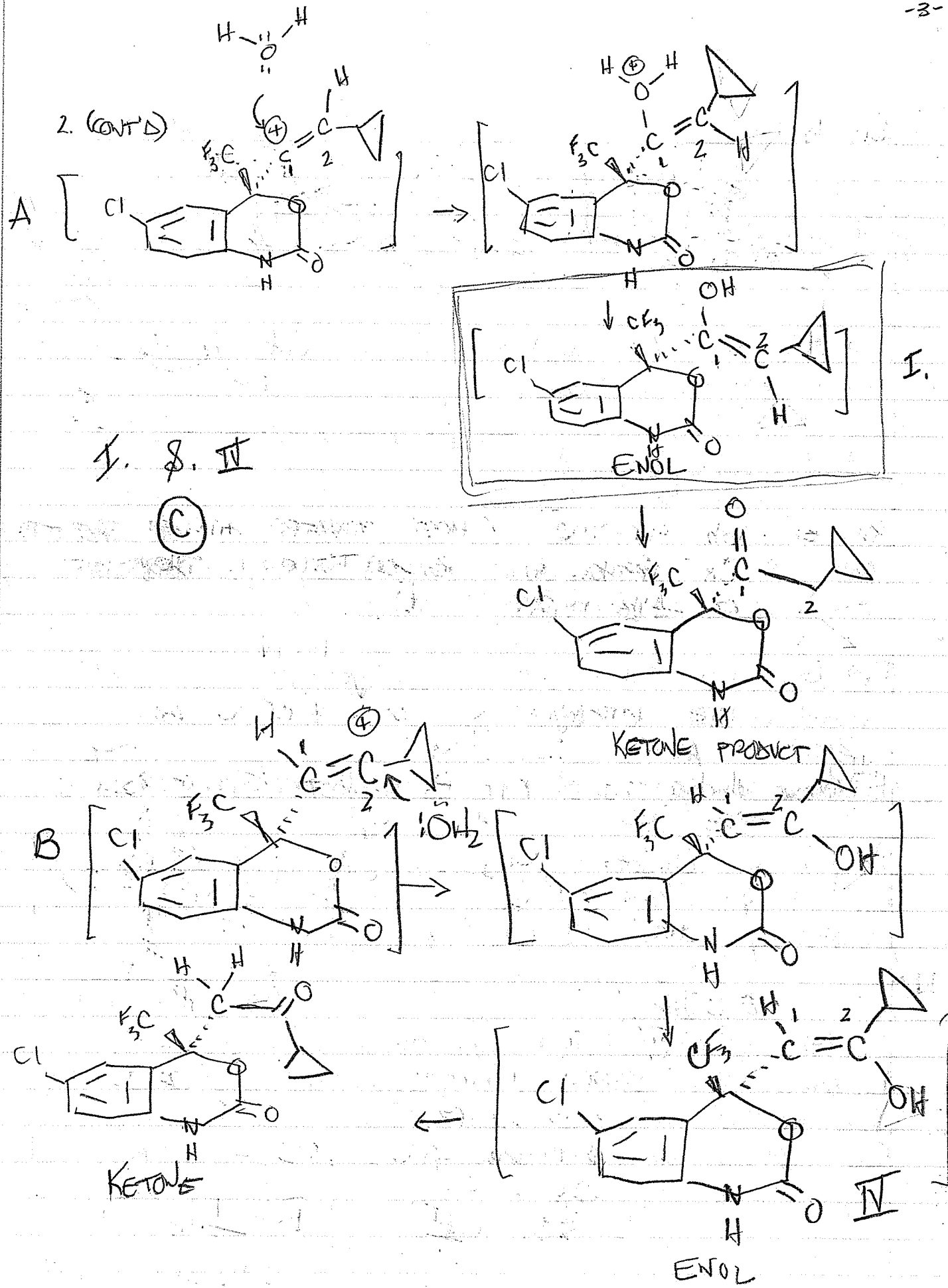
I. IS FORMED VIA TWO PATHWAYS, WHEREAS ALL OF THE OTHER COMPOUNDS ARE FORMED VIA ONLY ONE PATHWAY. THEREFORE I. IS THE MAJOR PRODUCT (A)

REACTION OF THE INTERNAL ALKYNE WITH H_3O^+ IS AN ELECTROPHILIC ADDITION THAT GIVES RISE TO TWO EQUALLY STABLE ENOLS, EACH THAT GIVES A KETONE. BOTH KETONES ARE MAJOR PRODUCTS OF THE RXN



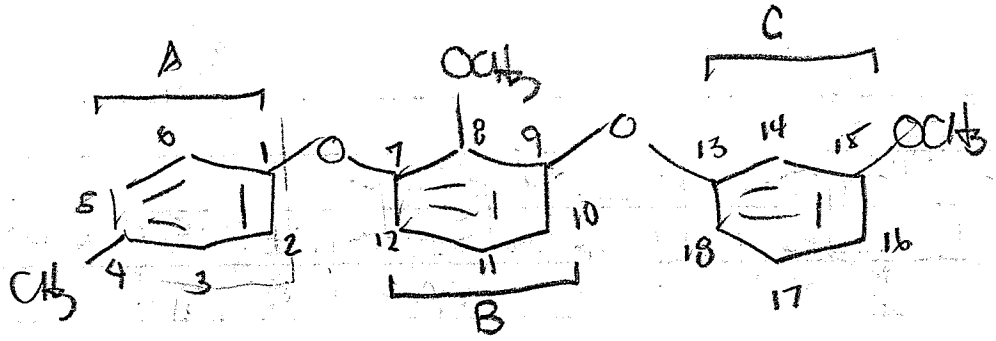
π e⊖ of alkyne react w/ H⊕ to generate two equally stable carbocations

2. (CONT'D)



1. 8. IV

C



dentify MOST ACTIVATED RING. That will determine where the rst chlorination occurs.

NG. A:	C_1	PHENOXY (A)	3RD MOST ACTIVATED	−0.21
	C_4	METHYL (A)		−0.17
				$\boxed{-0.38}$
NG B:	C_7	PHENOXY (A)	MOST ACTIVATED RING	−0.21
	C_8	METHOXY (A)	RXN OCCURS ON RING B	−0.21
	C_9	PHENOXY (A)	1st.	−0.27
				$\boxed{-.69}$
NG C:	C_{13}	PHENOXY (A)	2nd MOST ACTIVATED BASED	−0.21
	C_{15}	METHOXY (A)	ON SUM OF σ_p VALUES	−0.27
				$\boxed{-0.48}$

ermine which carbon of ring B is Most ACTIVATED

Phenoxy directs to C_{10}, C_{12}
Methoxy directs to C_{11}
Phenoxy directs to C_{10}, C_{12}

Rxn occurs @ C_{10}, C_{12}

$\boxed{C_{12} \text{ PRODUCT IS } \underline{III}}$

C_{10} PRODUCT NOT SHOWN

A = III

then reacts w/ Cl_2, $FeCl_3$ on RING C

ermine which carbon of ring C is Most ACTIVATED

3 Phenoxy directs to C_{18} and C_{16}
5 Methoxy directs to C_{18} and C_{16}

$$\underline{III} \xrightarrow[FeCl_3]{Cl_2} \underline{IV}$$

B = IV

3. (cont'd)

Determine which carbon of ring A reacts

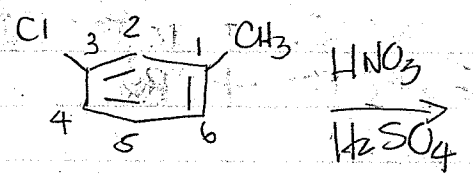
C_1 Phenoxy directs to C_2, C_6 $\sigma_p = -0.21$ <= MORE ACTIVATING

C_4 Methyl directs to C_3, C_5 $\sigma_p = -0.17$

C = VI

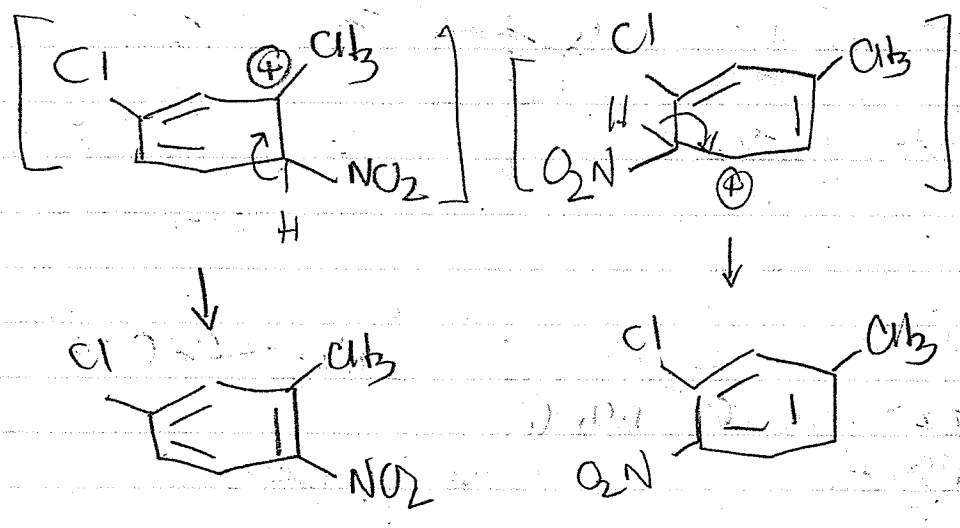
A = III B = IV C = VI (B)

4. I.



C_1 CH_3 ACTIVATOR o, p-DIRECTOR Directs rxn to C_4 ; C_6

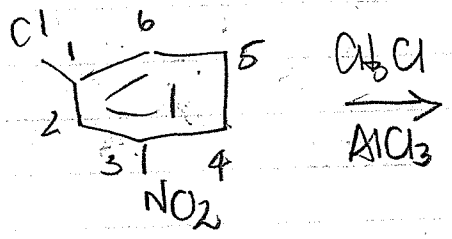
C_3 Cl DEACTIVATOR



NEITHER OF THESE IS INTERMEDIATE SHOWN

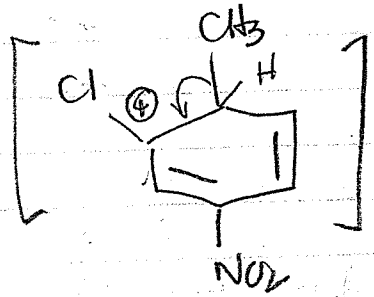
(CONT'D)

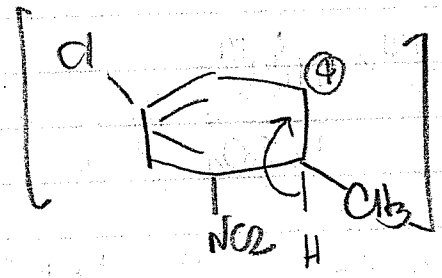
II.



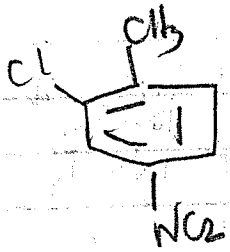
C_1 Cl (D) $\sigma_p = 0.23$ ⇐ Directs rxn since less deactivating directs to C_4, C_6 (o, p-director)

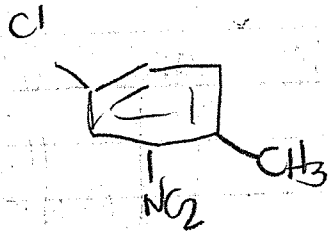
C_3 NO_2 (D) $\sigma_p = +0.78$





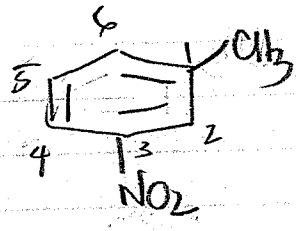
NEITHER ARE THE RXN INTERMEDIATE SHOWN





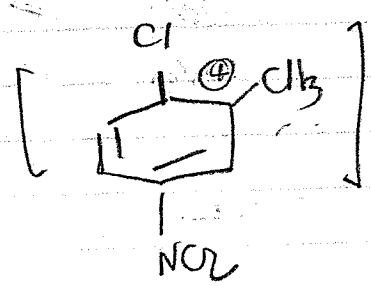
(E)

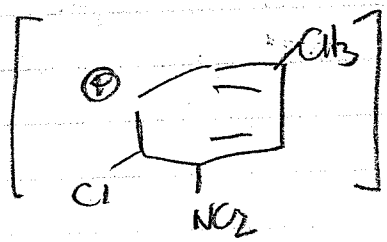
III.



C_1 CH_3 (A) directs to C_4, C_6

C_3 NO_2 (D)

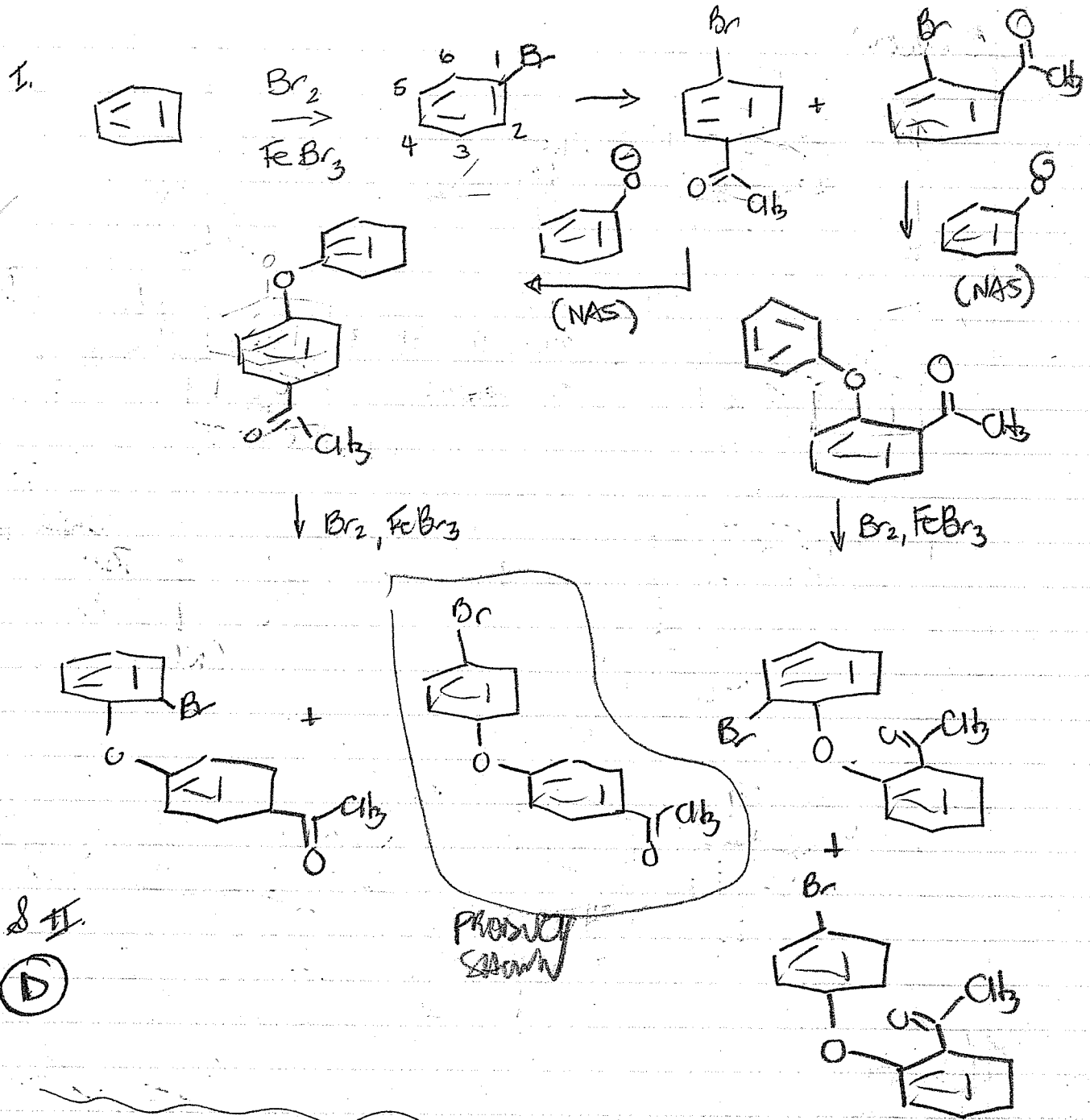




Neither are the intermediate shown

5.

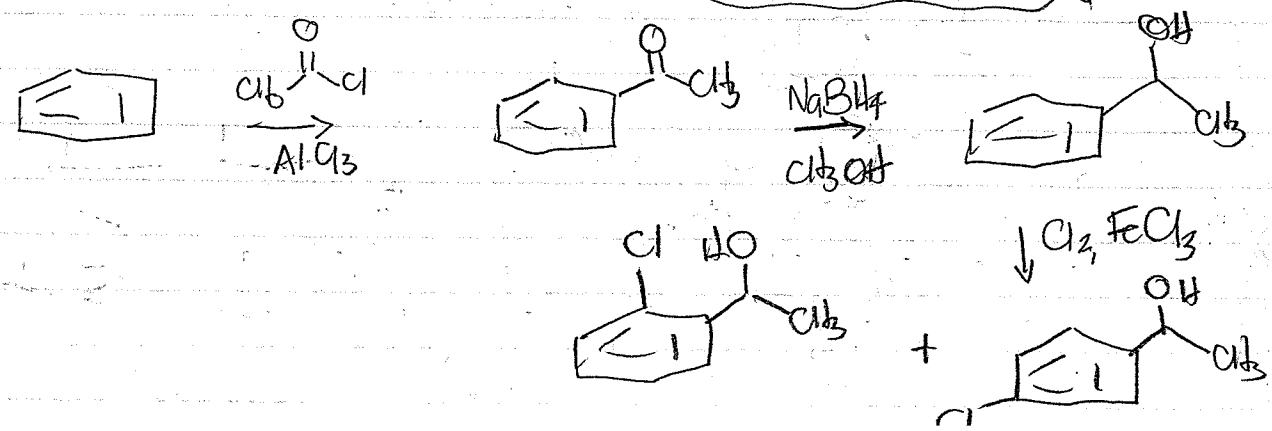
I.


Br_2
$FeBr_3$
(NAS)
(NAS)
$Br_2, FeBr_3$
$Br_2, FeBr_3$
Product shown

I & II.

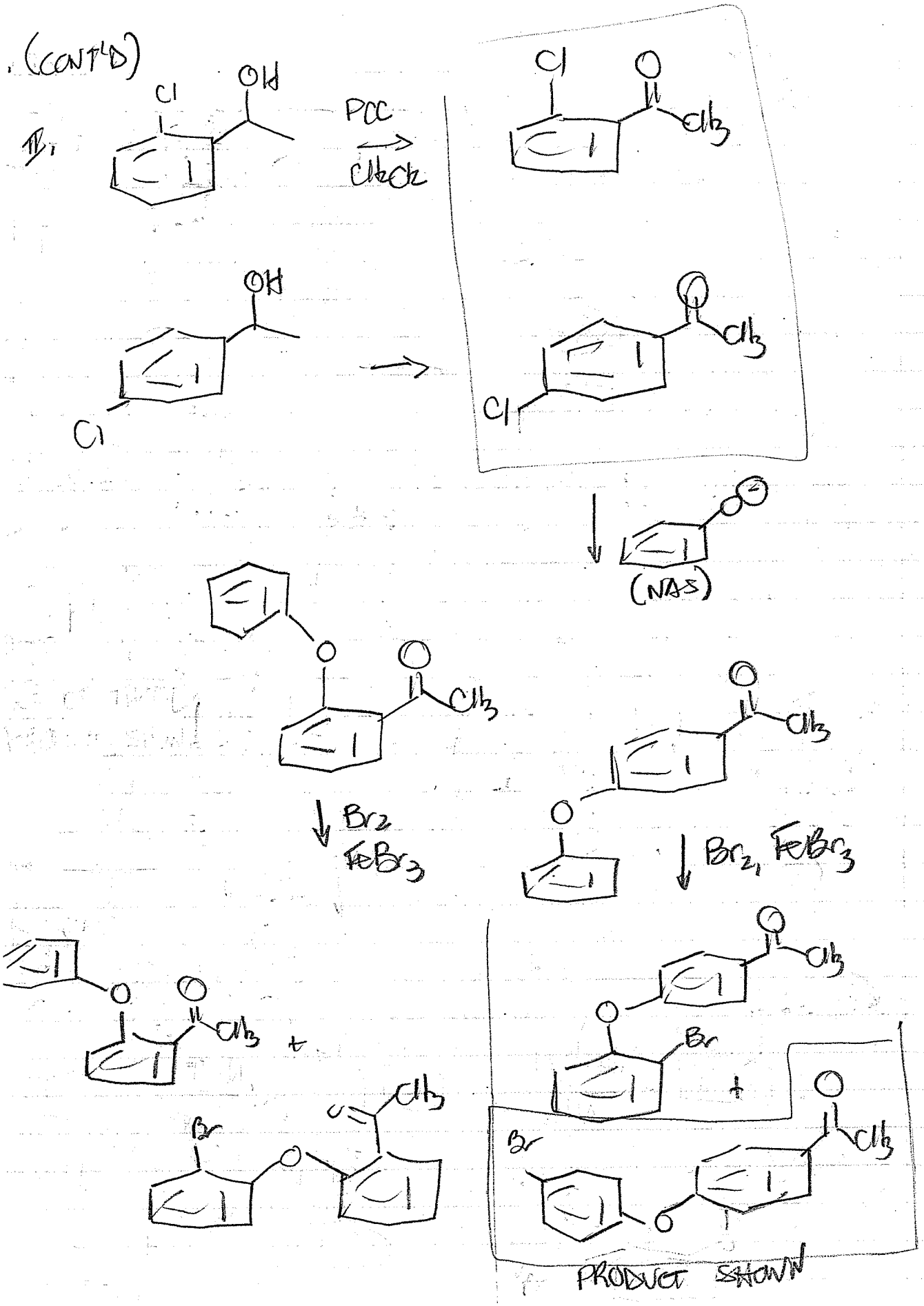
D

II.


$AlCl_3$
$NaBH_4$
CH_3OH
$Cl_2, FeCl_3$

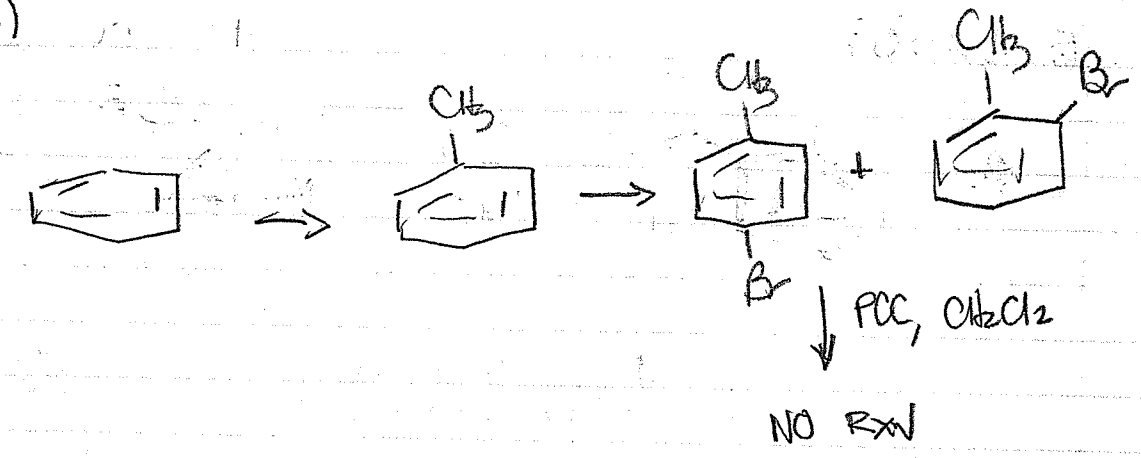
(CONT'D)

II.

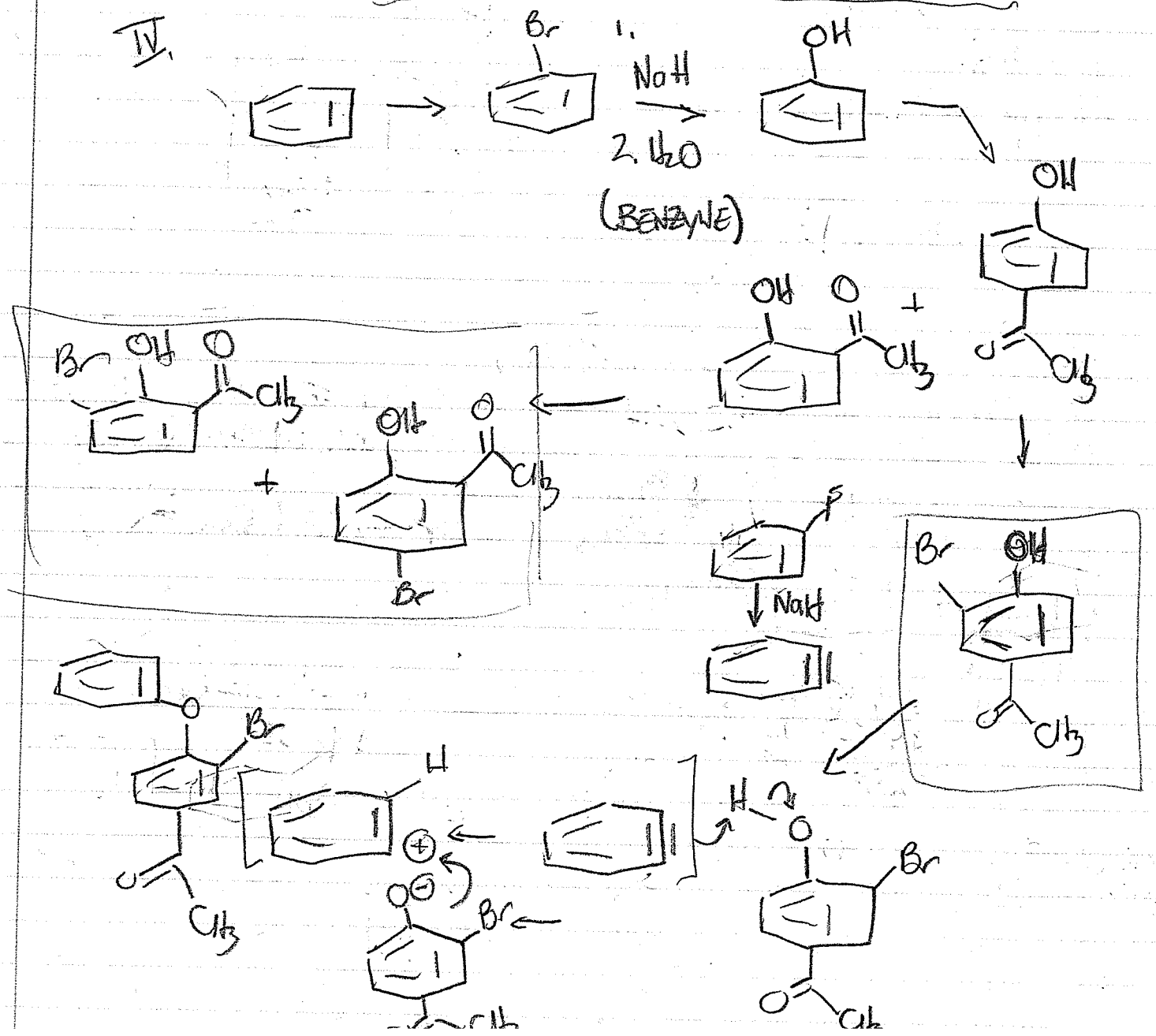


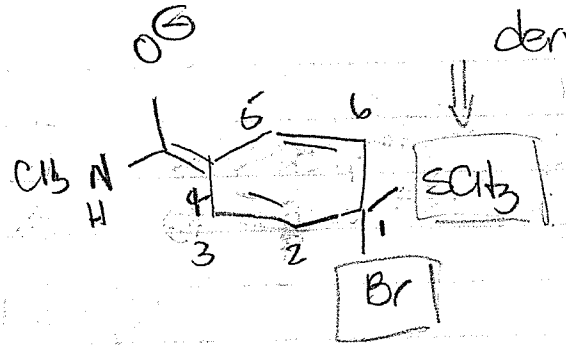
5. (CONT'D)

III.



IV.

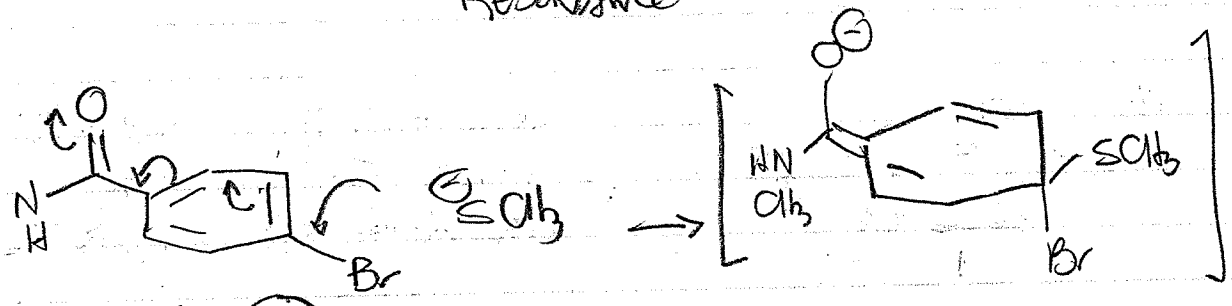




derived from the nucleophile $CH_3S^{\ominus}$ $Na^{\oplus}$

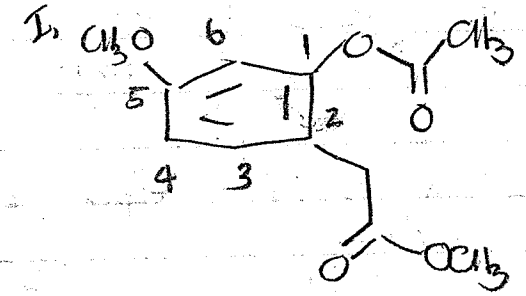
Nu: Aromatic Substitution

LEAVING GROUP PARA TO ENG BY RESONANCE



III. (A)

I.



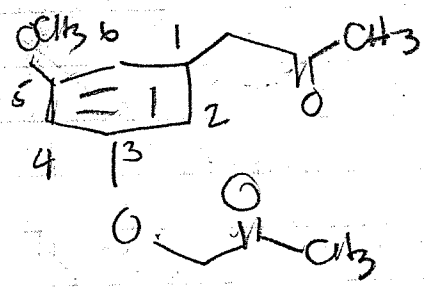
C1 ACETOXY (A) $\sigma_p = -0.01$

C2 $-CH_2C(=O)OCH_3$ (METHYL) (A) $\sigma_p = -0.17$

C5 METHOXY (A) $\sigma_p = -0.27$

$\boxed{-0.45}$

II.

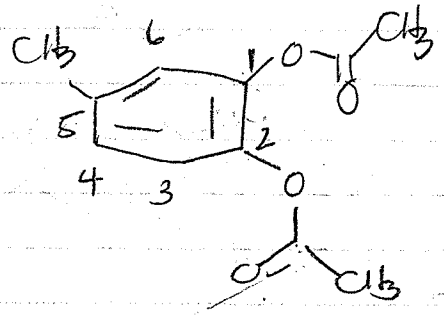


ALL POSITIONS STERICALLY BLOCKED

I > II

7. (cont'd)

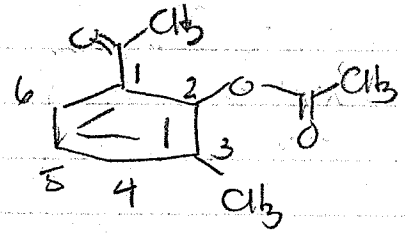
III.



C_1	ACETOXY (A)	$\sigma_p = -0.01$
C_2	ACETOXY (A)	$\sigma_p = -0.01$
C_5	METHYL (A)	$\sigma_p = -0.17$
		$\boxed{-0.19}$

I > III > II

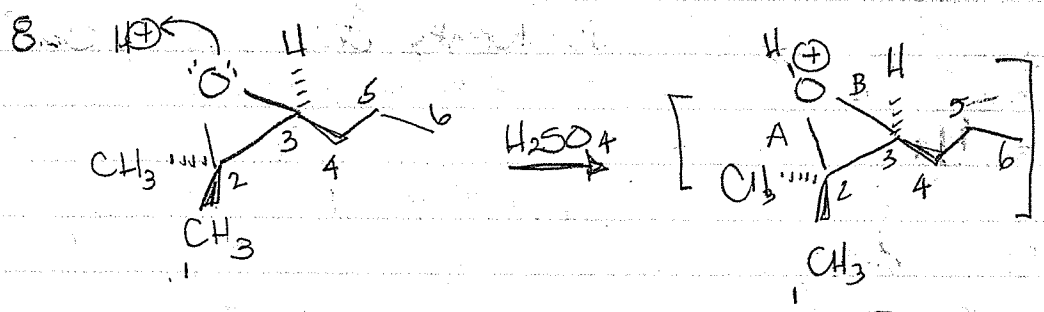
IV.



C_1	ACETYL (D)	$\sigma_p = +0.5$
C_2	ACETOXY (A)	$\sigma_p = -0.01$
C_3	METHYL (A)	$\sigma_p = -0.17$

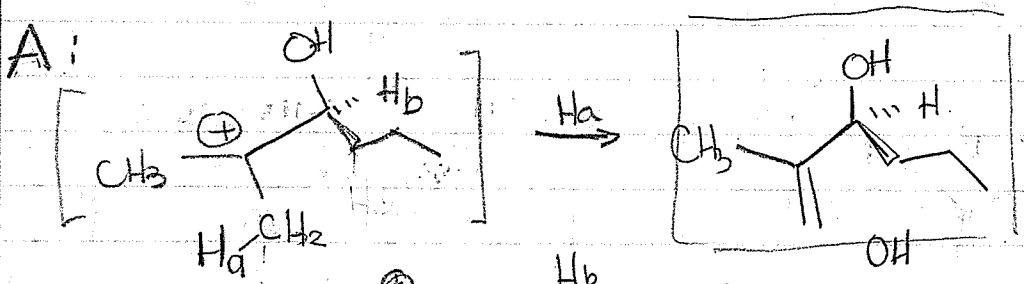
I > III > IV > II (C)

8.



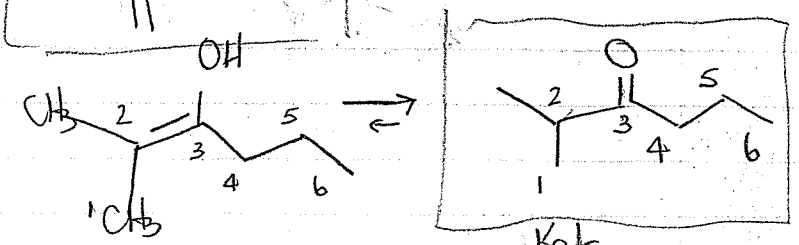
CONSIDER BREAKING A BOND and B BOND

A:



Allylic alcohol I.

3° ALKYL $C^{\oplus}$

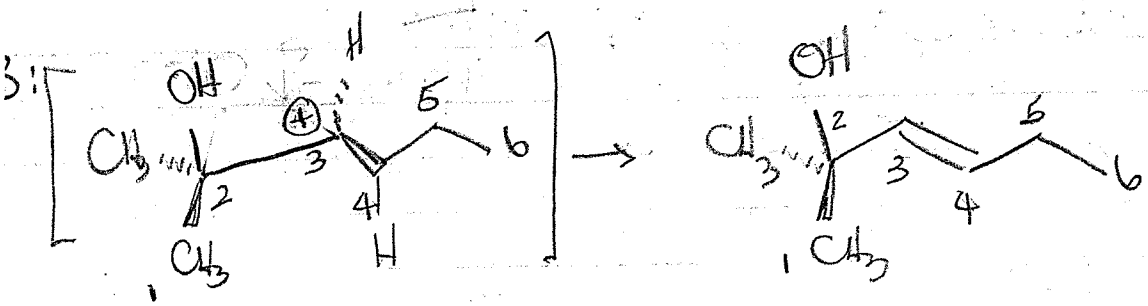


Ketone II.

Both the allylic alcohol and ketone are both derived from 3° carbocation

(CONT'D)

3:



III.

2° ALKYL CARBOCATION

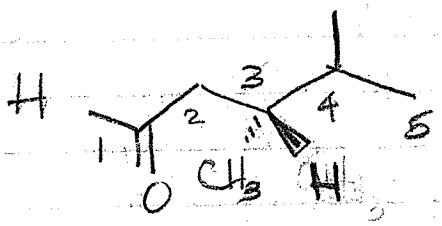
The only adjacent H is at C_4. No H @ C_2 to form enol

I & II derived from more stable 3° carbocation and are BOTH major kinetic products

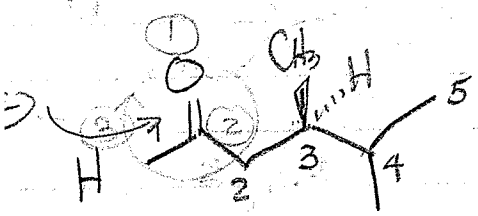
A

3R-3,4-dimethylpentanal

To identify Re face, orient aldehyde so substituents are clockwise

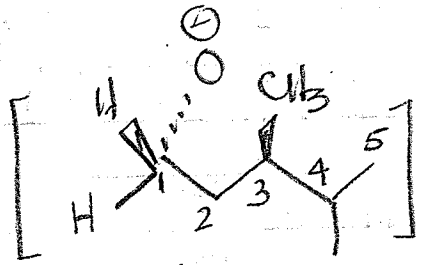


↓ FLIP OVER



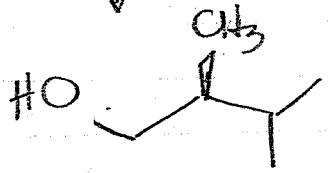
CLOCKWISE

RE IS FRONT



D

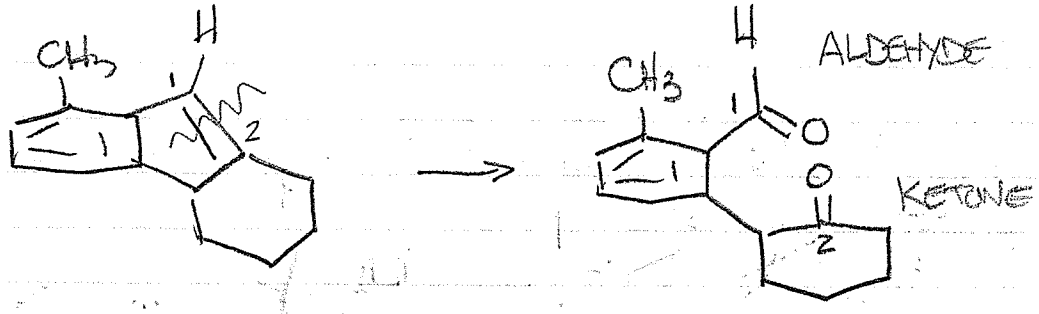
↓



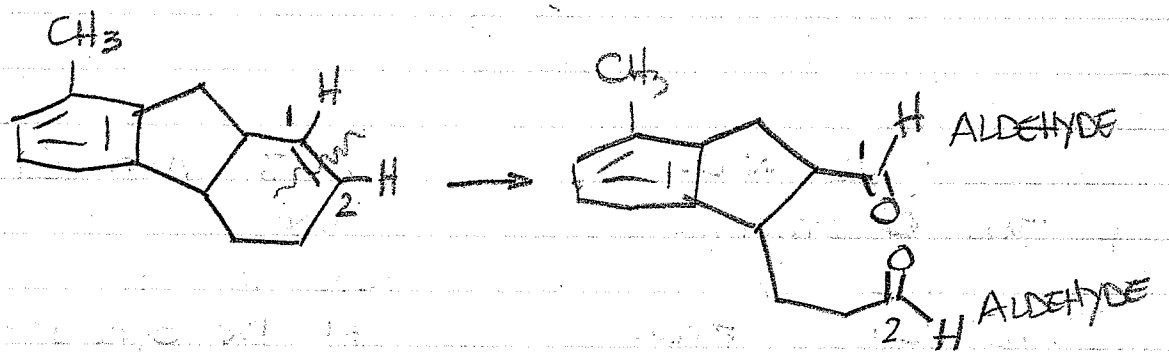
SINGLE PRODUCT W/ R CONFIGURAT

10.

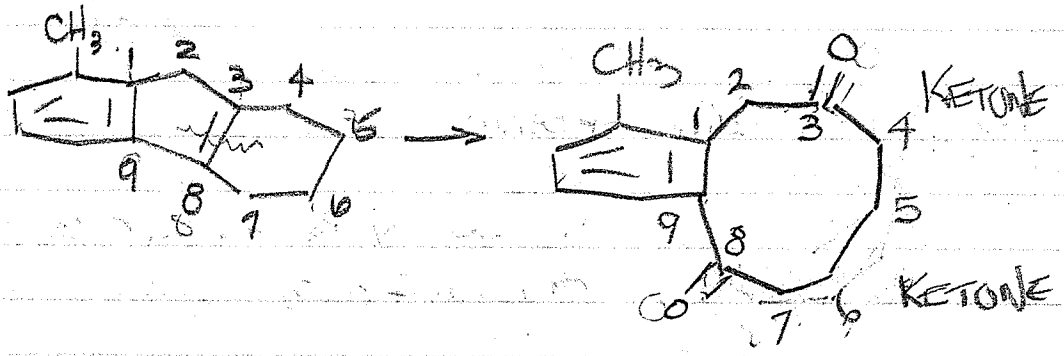
I.



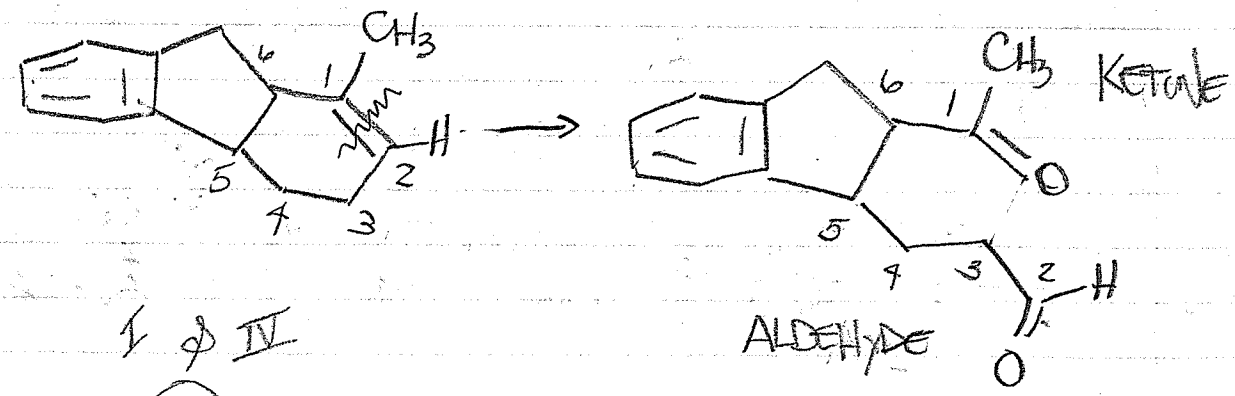
II.



III.



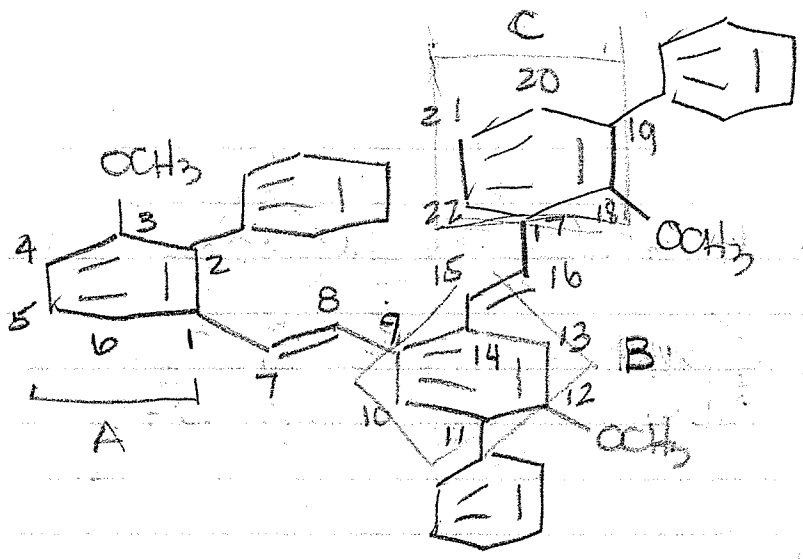
IV.



I & IV

A

1.



Most stable $C^{\oplus}$ has ring with EDG (↑ ⊖ on RING)

↑ RATE OF RXN (FASTER)

CARBOCATIONS WILL FORM AT C_7-C_8 AND C_{15}-C_{16} IN THE ELECTROPHILIC ADDITION

$C^{\oplus}$ @ C_7 : stability influenced by substituents on ring A

I.

$\boxed{\sigma_{sum} = +0.11}$

C_2: Phenyl ORTHO to $C^{\oplus}$ @ C_7
$\sigma_p = -0.01$

C_3: Methoxy META to $C^{\oplus}$ @ C_7
$\sigma_m = +0.12$

$C^{\oplus}$ @ C_8 : stability influenced by substituents on ring B

II.

$\boxed{\sigma_{sum} = -0.23}$

C_{11}: Phenyl META to $C^{\oplus}$ @ C_8 $\sigma_m = +0.06$
C_{12}: Methoxy PARA to $C^{\oplus}$ @ C_8 $\sigma_p = -0.27$
C_{14}: Alkenyl ORTHO to $C^{\oplus}$ @ C_8 $\sigma_p = -0.02$

11. (CONT'D)

$C^{\oplus}$ @ C_{15}: stability influenced by substituents on ring B

IV.

$\boxed{\sigma_{SUM} = -0.3}$

C_9: Alkenyl ORTHO to $C^{\oplus}$ $\sigma_p = -0.02$
C_{11}: Phenyl PARA to $C^{\oplus}$ $\sigma_p = -0.01$
C_{12}: Methoxyl META to $C^{\oplus}$ $\sigma_m = -0.27$

D

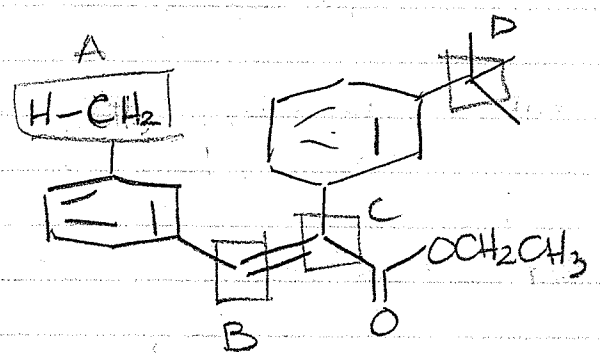
$C^{\oplus}$ @ C_{16}: stability influenced by substituents on ring C

$\boxed{\sigma_{SUM} = -0.21}$

III.

C_{18} Methoxy ORTHO to $C^{\oplus}$ $\sigma_p = -0.27$
C_{19} Phenyl META to $C^{\oplus}$ $\sigma_m = +0.06$

12.



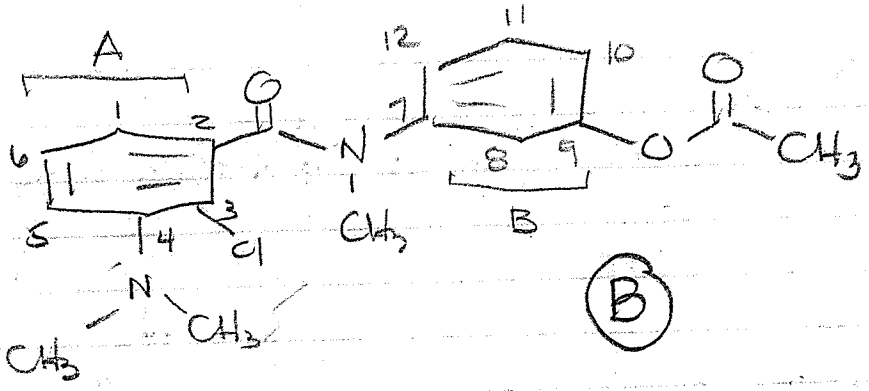
NBS, hν reacts @ BENZYLIC sp^3 carbons bonded to at least one H atom

Positions labeled as A, B, C, D are all benzylic.
But ONLY A is sp^3 and bonded to at least 1 H

H @ A position is substituted w/ Br in benzylic bromination.

E

3.



(B)

I. TRUE
II. TRUE
III. FALSE
IV. FALSE
V. FALSE

RING A C2 $-C(=O)-N(CH_3)-$ ACETYL EWG by RESONANCE

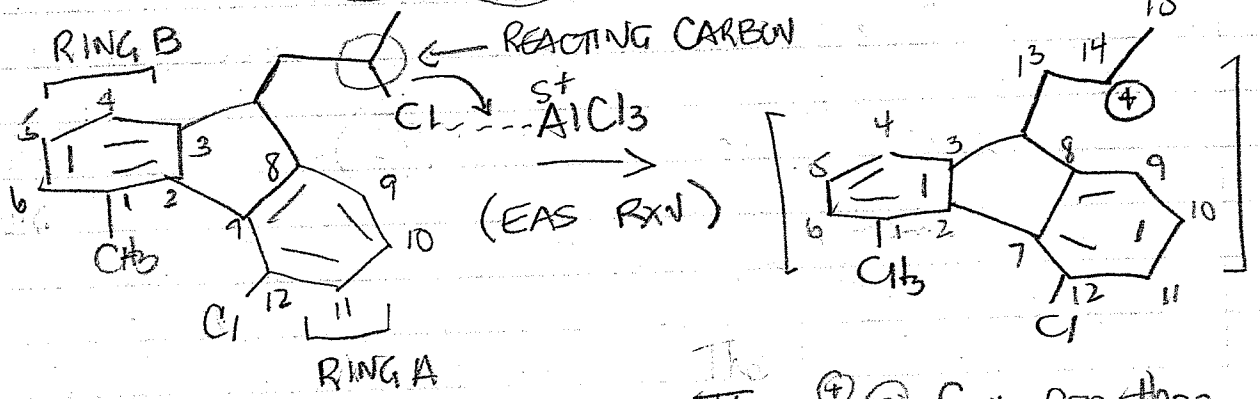
C4 $-N(CH_3)_2$ AMINO EWG by INDUCTION
EDG by RESONANCE

C3 Cl CHLORO EWG by INDUCTION
EDG by RESONANCE

RING B C9 $-NH-C(=O)-$ ACETAMIDO EDG by RESONANCE
EWG by INDUCTION

C9 $-O-C(=O)-$ ACETOXY EDG by RESONANCE
EWG by INDUCTION

14.



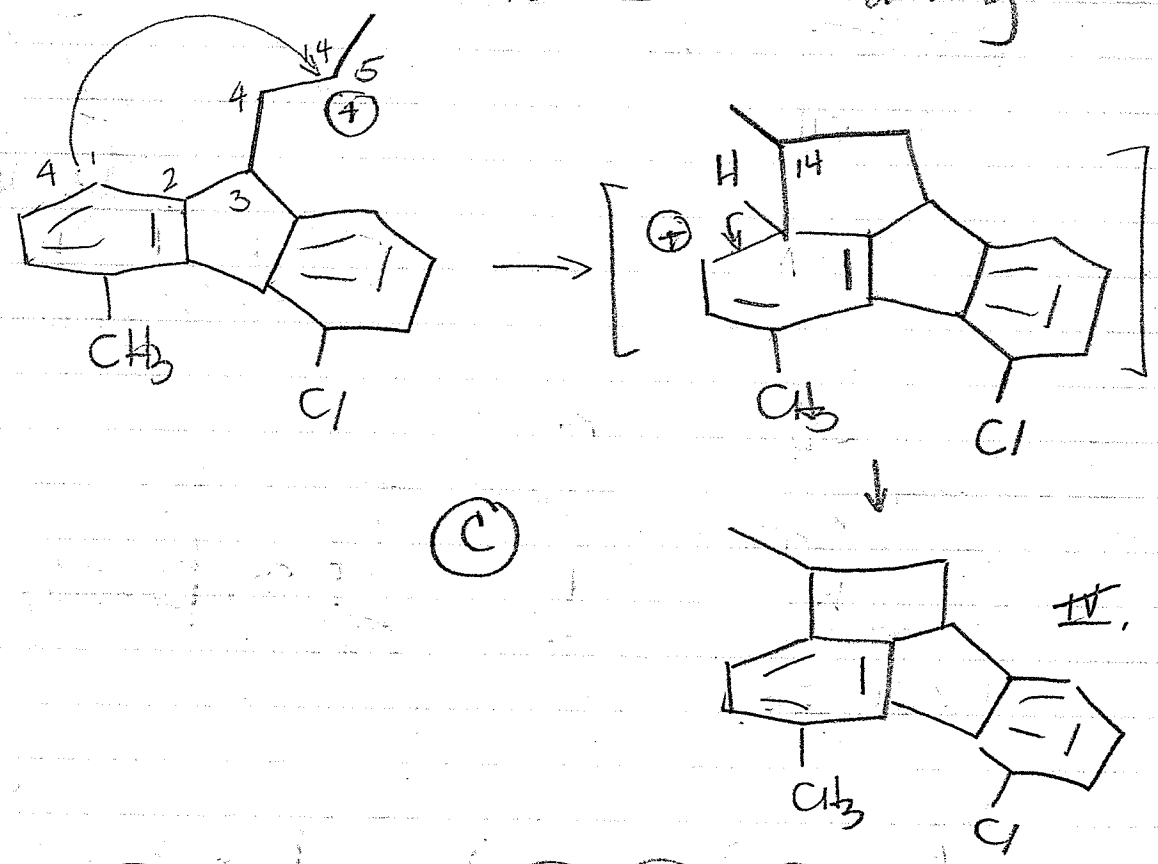
Ring B: C1 CH_3 (A) directs to C4

Ring B C12 Cl (D) directs to C9

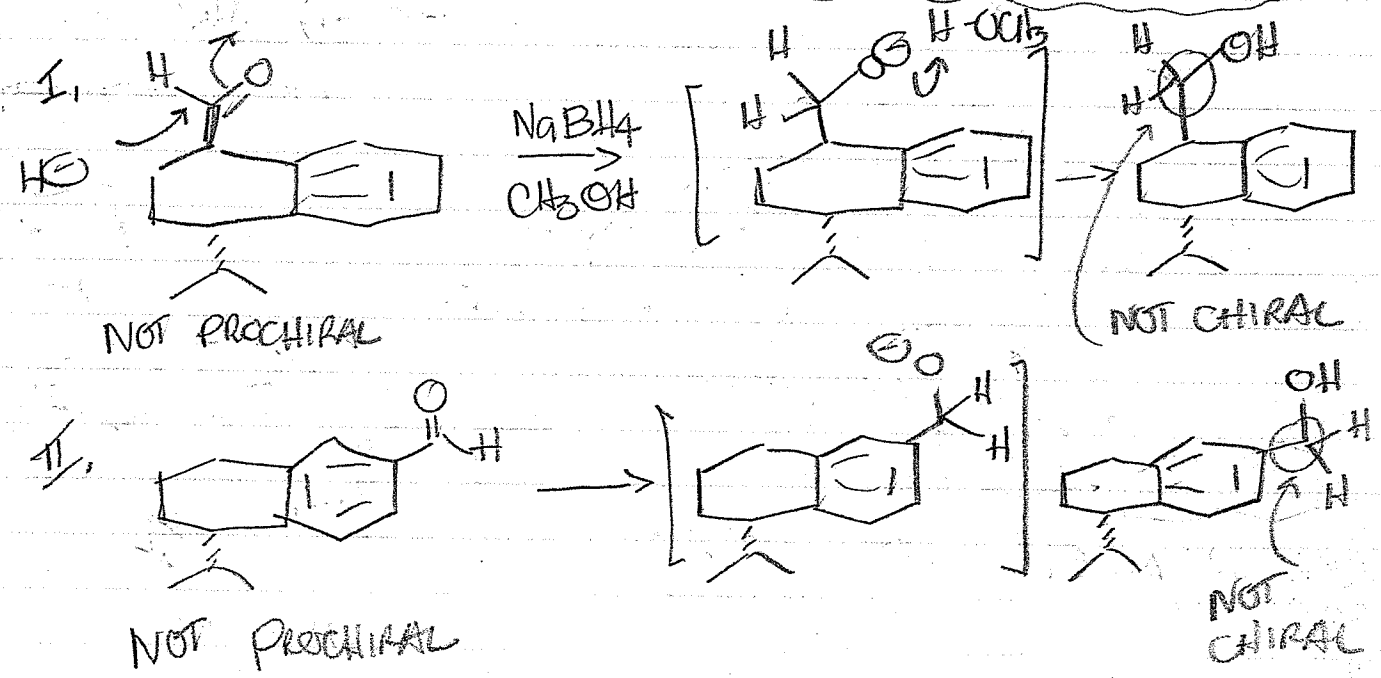
The ⊕ @ C14 can then react in a Friedel-Crafts alkylation (INTRAMOLECULAR) on ring A or ring B. Ring B is more activated

14. (CONT'D)

Rxn w/ $C^{\oplus}$ occurs @ C_4. Rxn results in formation of new 5-membered ring

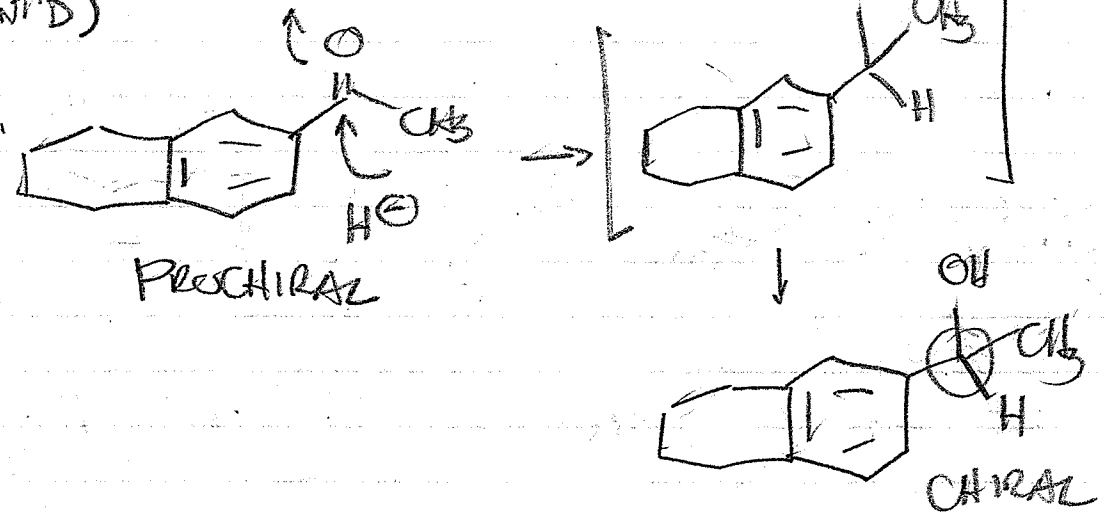


15.

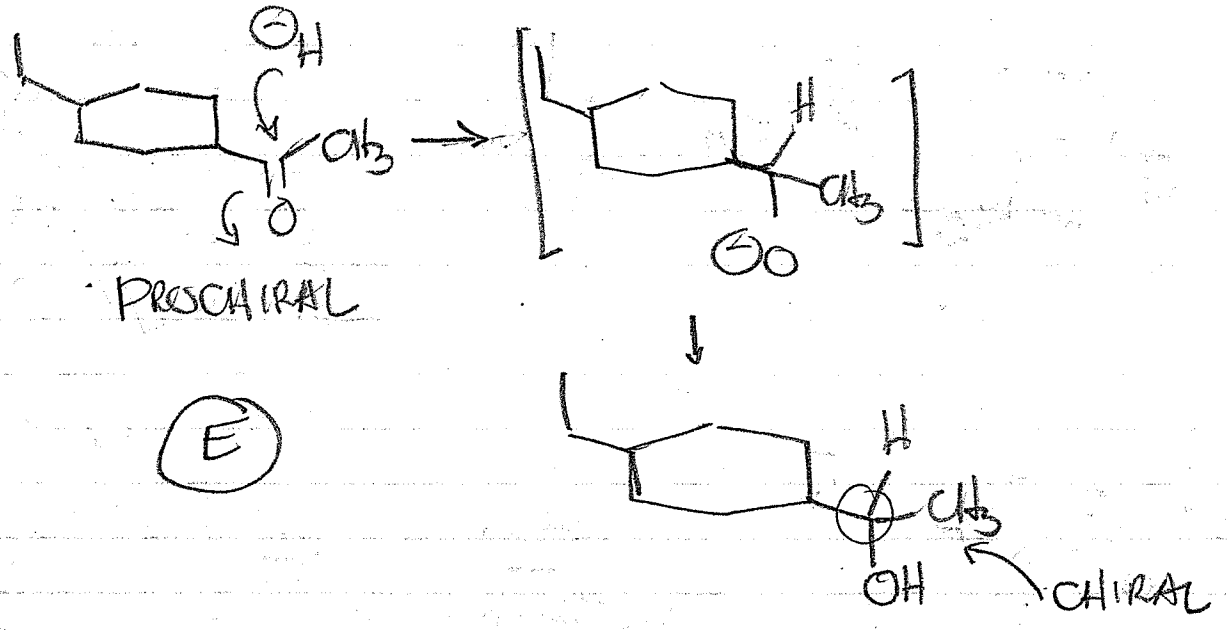


15. (CONT'D)

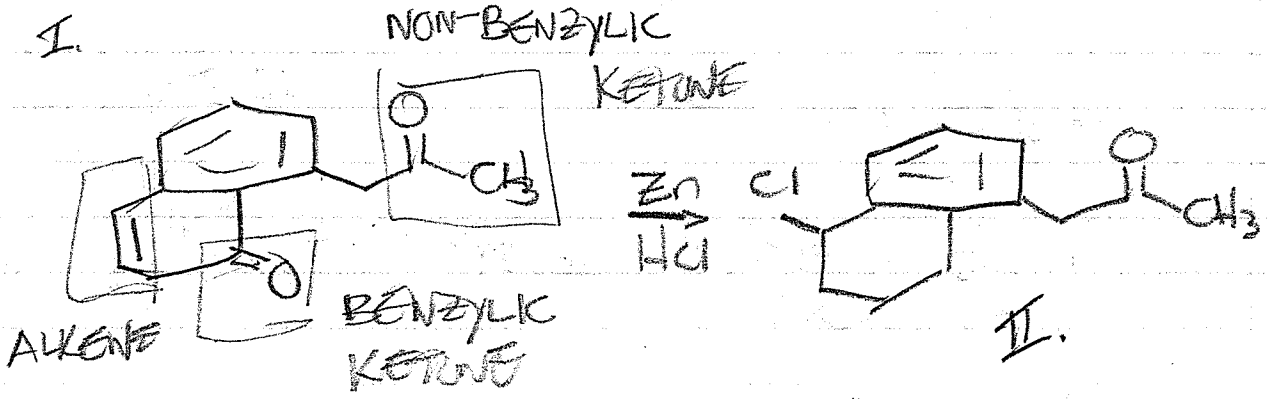
III.



IV.

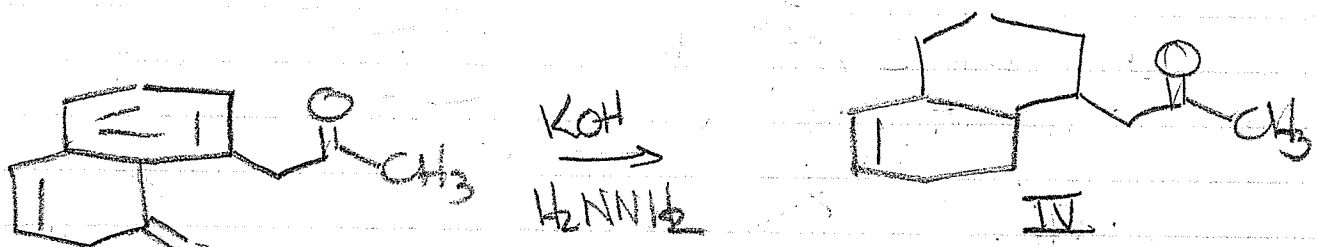


6. I.

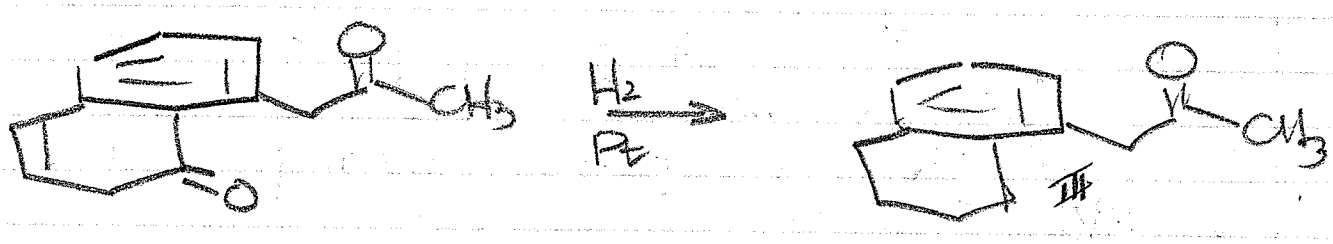


A = II

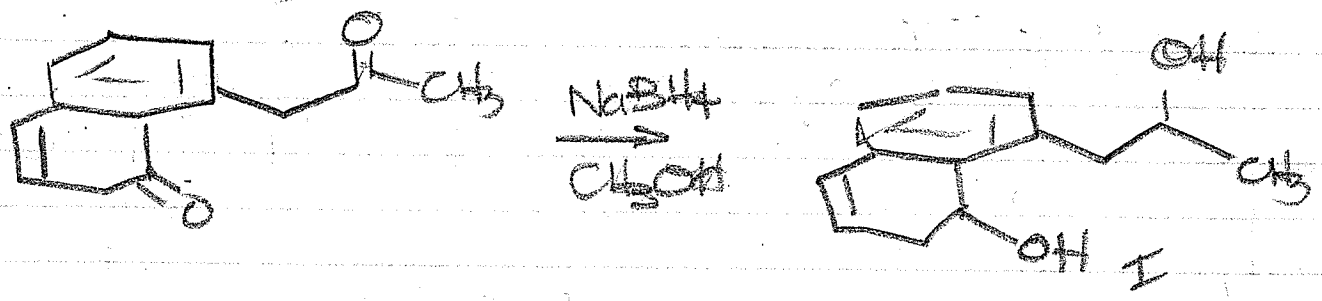
16. (CONT'D)



B = IV



C = III

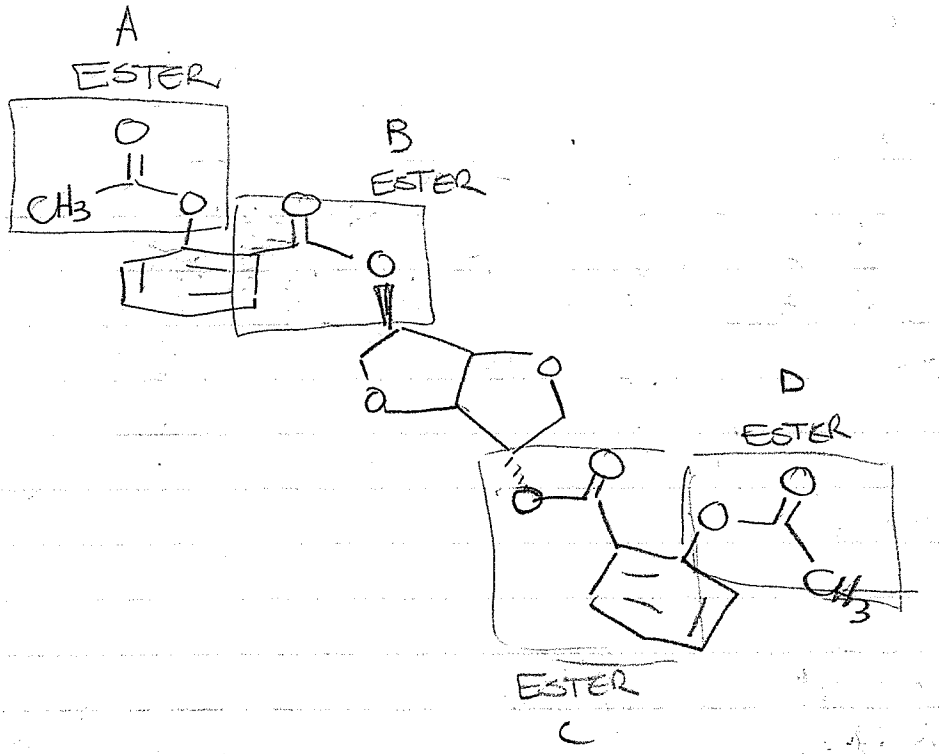


D = I

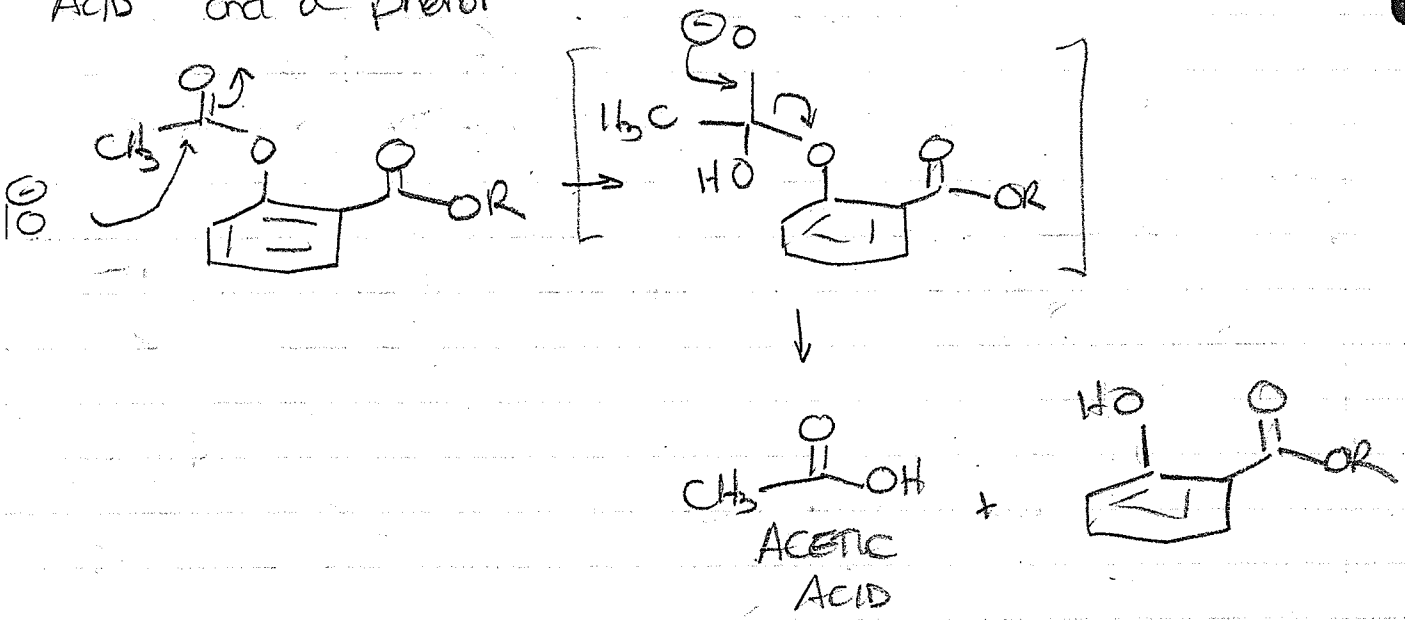
A = II B = IV C = III D = I

A

17.

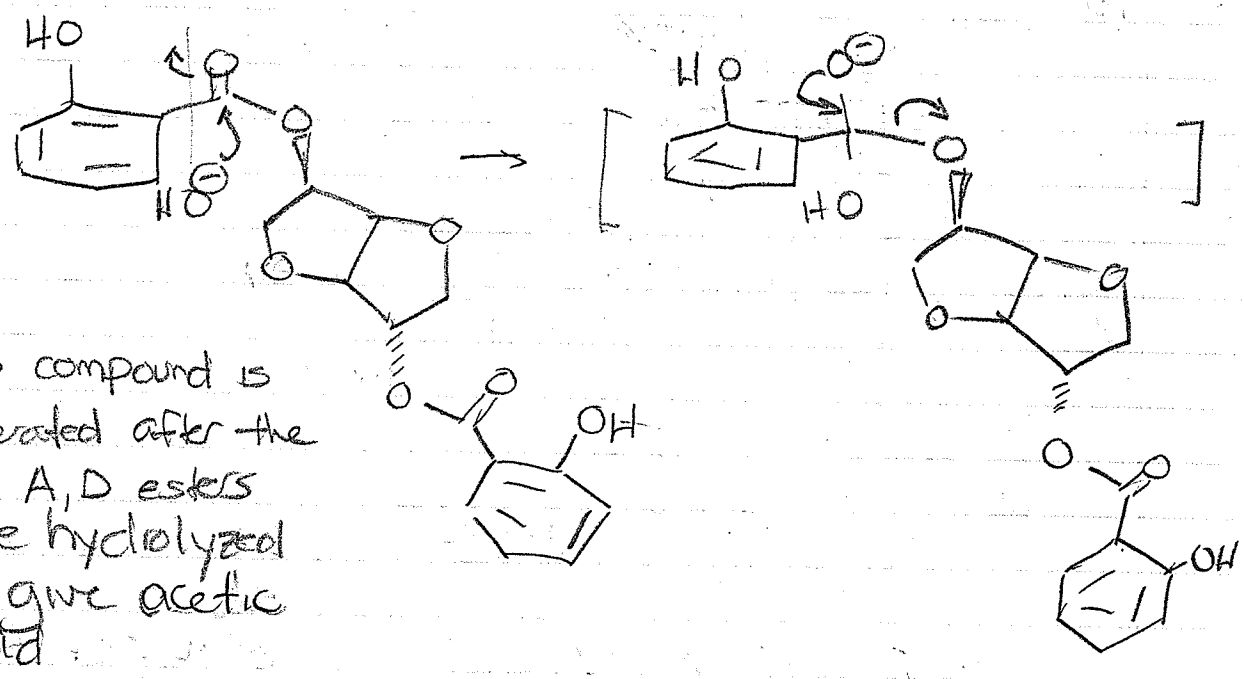


Esters A and D undergo hydrolysis to give Acetic Acid and a phenol

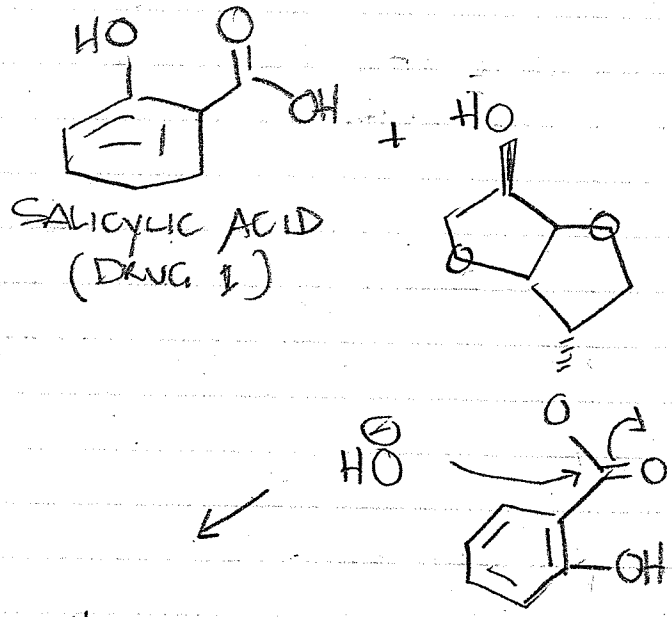


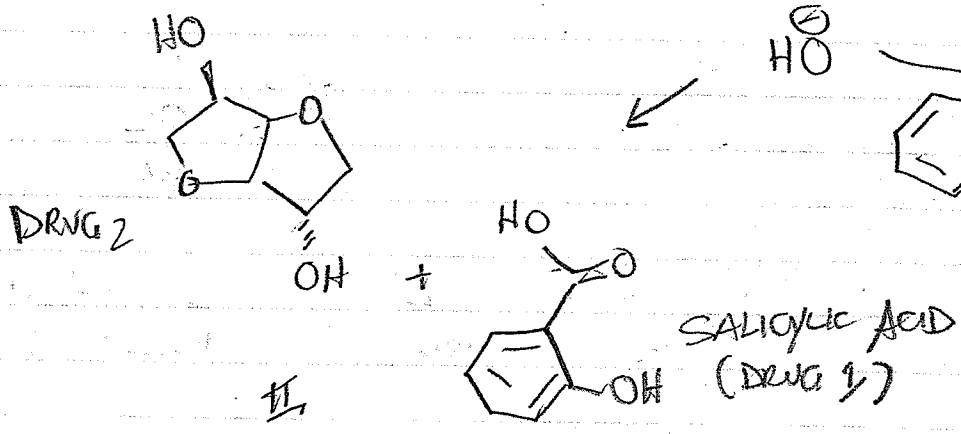
The remaining two esters B and C undergo hydrolysis to give the two active drugs

17. (CONT'D)



This compound is generated after the two A,D esters have hydrolyzed to give acetic acid.

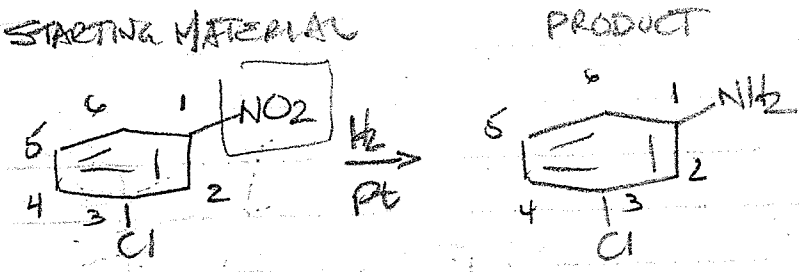




II.

C

3. I.

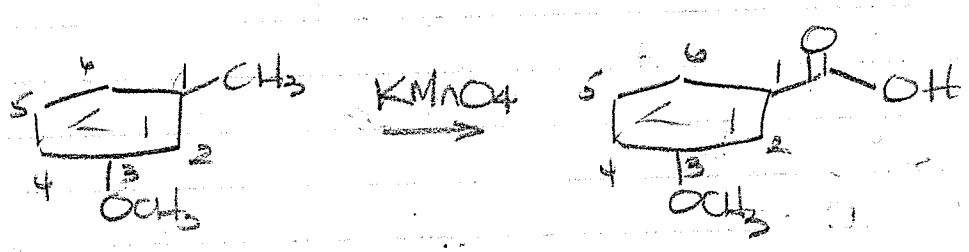


I & III

(D)

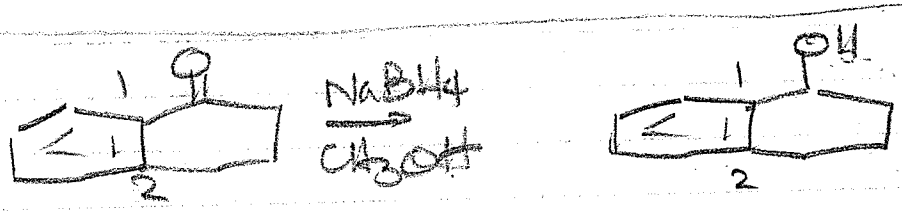
C_1	$-NO_2$	DEACTIVATOR	$-NH_2$	ACTIVATOR
C_3	$-Cl$	DEACTIVATOR	$-Cl$	DEACTIVATOR
			MORE REACTIVE THAN SM	

II.



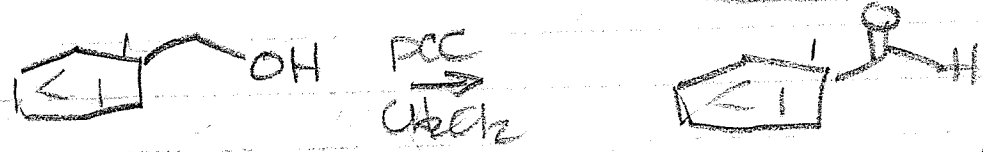
C_1	$-CH_3$	ACTIVATOR	C_1	$-\overset{O}{\overset{\|\|}{C}}-OH$ DEACTIVATOR
C_3	$-OCH_3$	ACTIVATOR	C_3	$-OCH_3$ ACTIVATOR
			LESS REACTIVE THAN SM	

III.



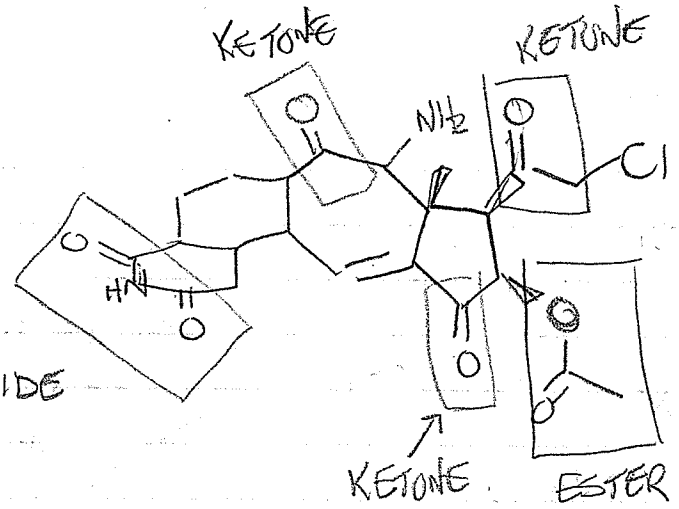
C_1	$-\overset{O}{\overset{\|\|}{C}}-$	DEACTIVATOR	C_1	$-CH-OH$ ACTIVATOR
C_2	$-CH_2$	ACTIVATOR	C_2	CH_2- ACTIVATOR
			MORE REACTIVE THAN SM	

IV.



C_1	$-CH_2$	ACTIVATOR	C_1	$-\overset{O}{\overset{\|\|}{C}}-$ DEACTIVATOR
			LESS REACTIVE THAN SM	

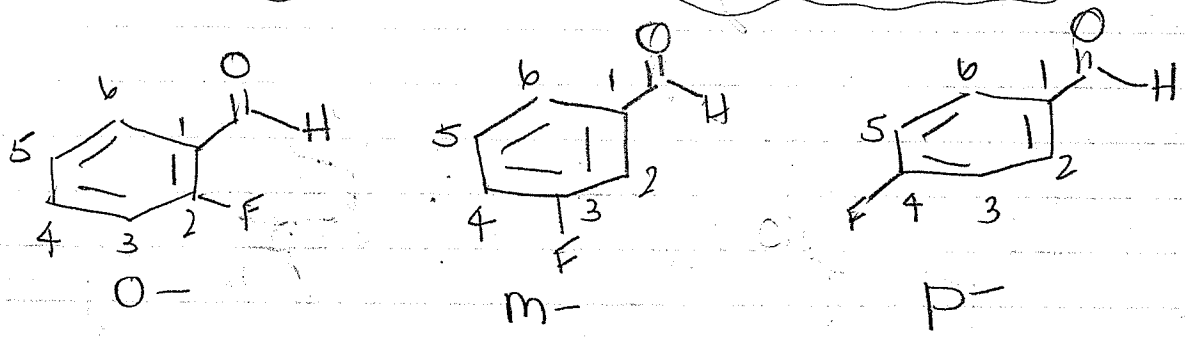
19.



II. KETONE
III. ESTER
V. IMIDE

II, III & V (B)

20.

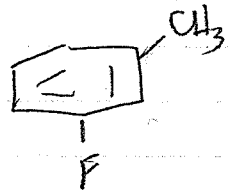


- F directs to C3, C5
- C-H directs to C3, C5
  ‖ O

I. FALSE

(B)

Rxn w/ Zn, HCl

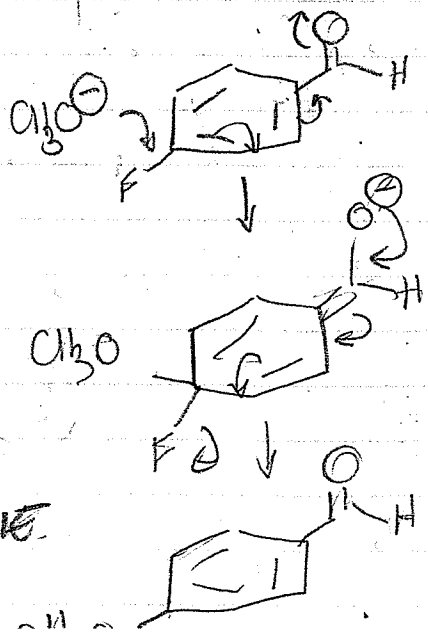


m-fluorotoluene

III. TRUE

LG = F para to
- C-H which is EWG
  ‖ O

by resonance
Rxn w/ CH_3O^-

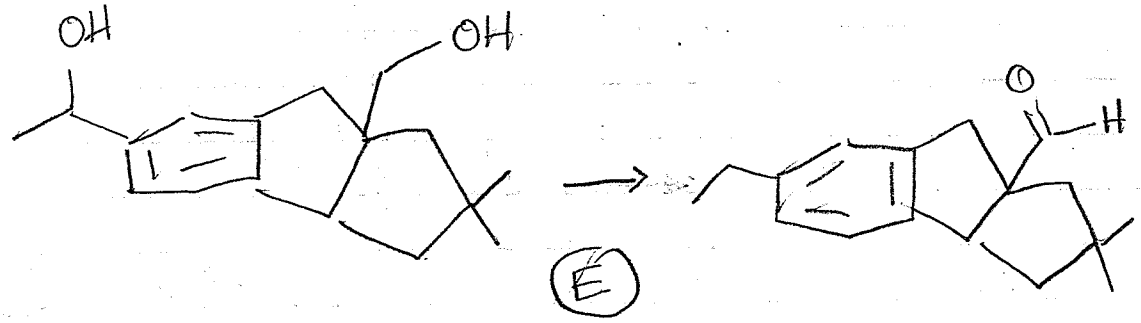


IV. DIBAL only reacts w/ esters
FALSE

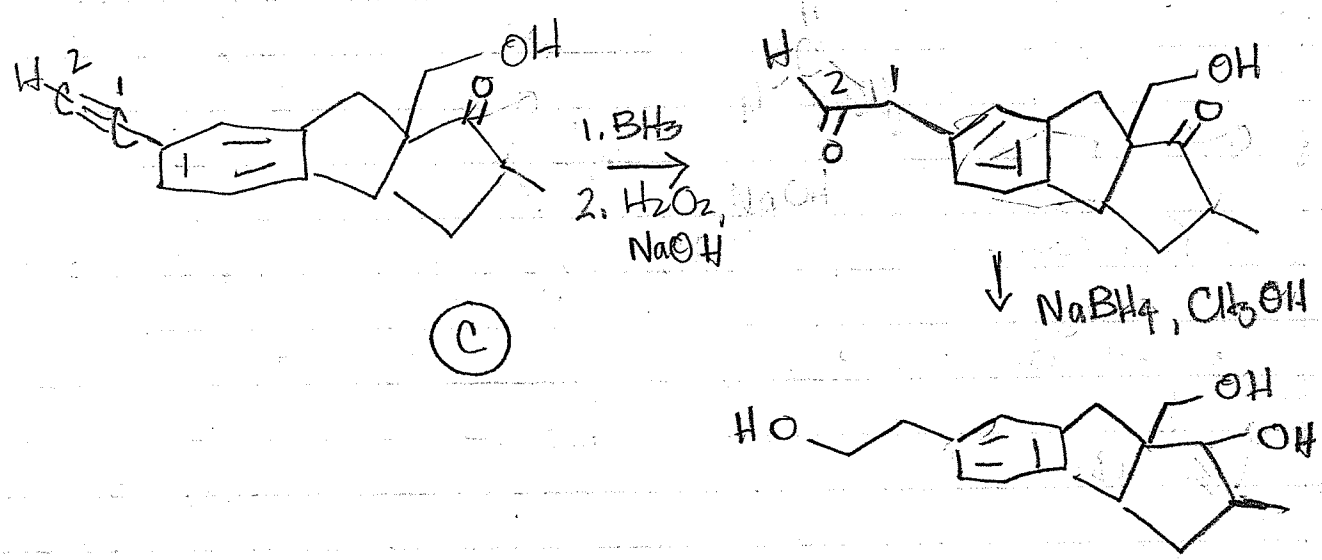
II. TRUE

p-methoxybenzaldehyde

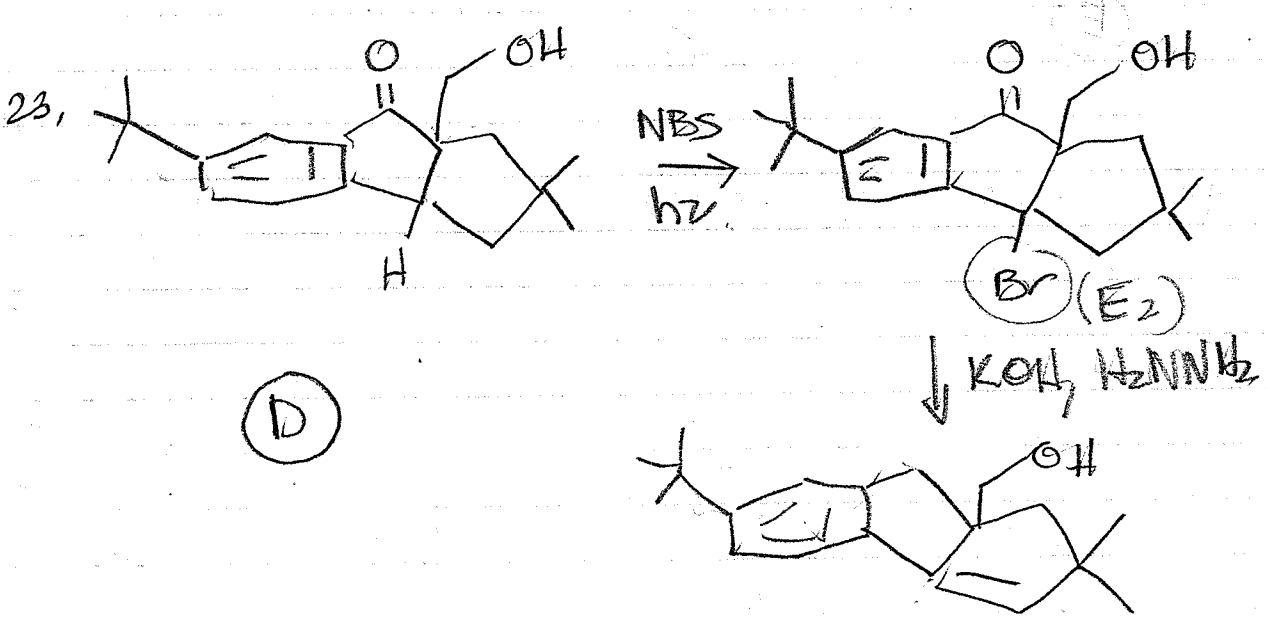
21.


OH
OH
O
H
E

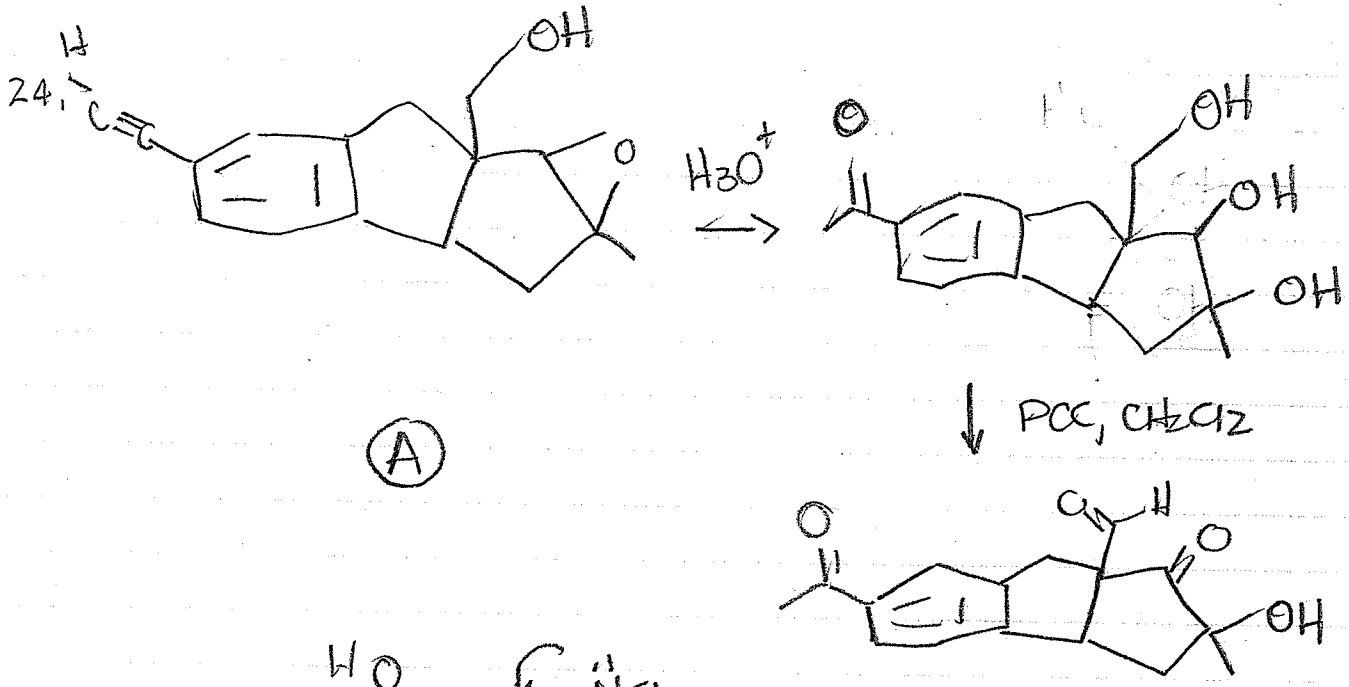
22.


H
2
1
OH
O
1. BH3
2. H2O2, NaOH
H
2
1
OH
O
O
C
NaBH4, CH3OH
HO
OH
OH

23.

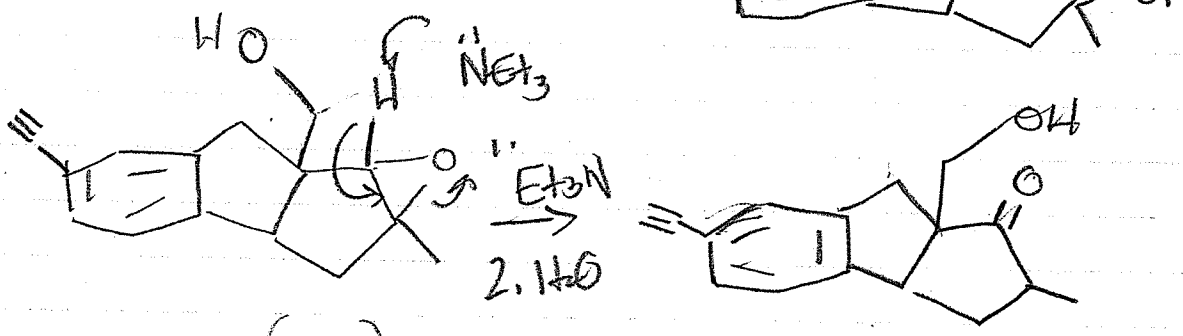

O
OH
H
NBS
hν
O
OH
Br
(E2)
KOH, H2NNH2
OH
D

24.


H
OH
O
H_3O^+
OH
OH
OH
PCC, CH_2Cl_2
O
H
O
OH

(A)

25.


HO
H
NEt_3
O
Et_3N
2. H_2O
OH
O
$NaBH_4$, CH_3OH
OH
OH

(E2)

(B)