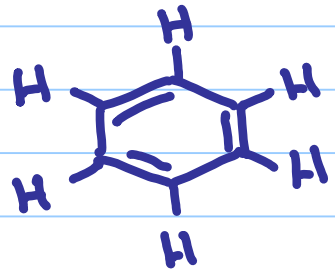
Lecture 1 - Orgo 2.

Note Title

In Karty
14.3 Energy of Hydrogenation
4n +2 Rule
14.7, 14.8, 14.9,14.10 1/5/2017
Aromaticity in non-benzenes

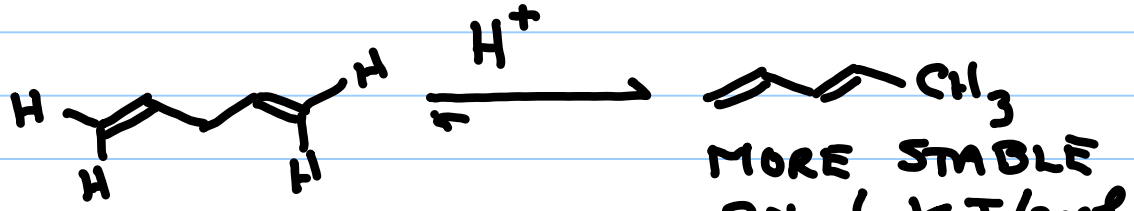
Aromatic Compounds

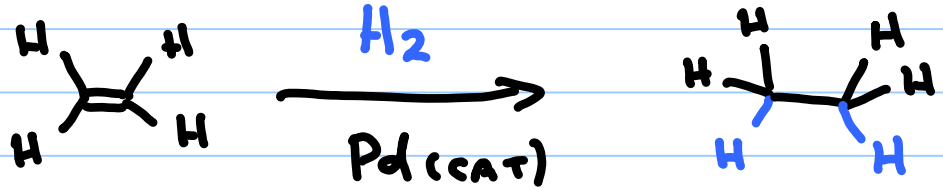


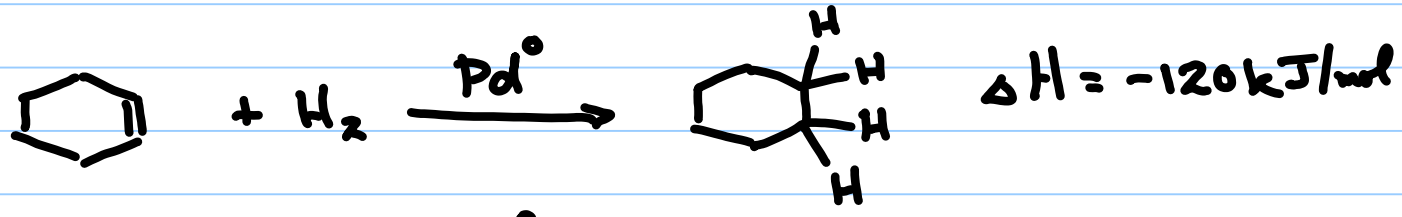
Benzene

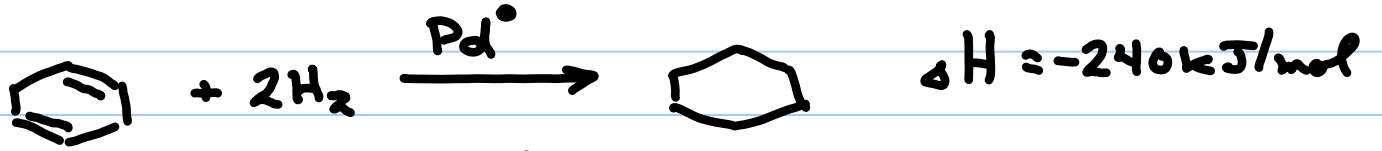
- What makes an Compound Aromatic?

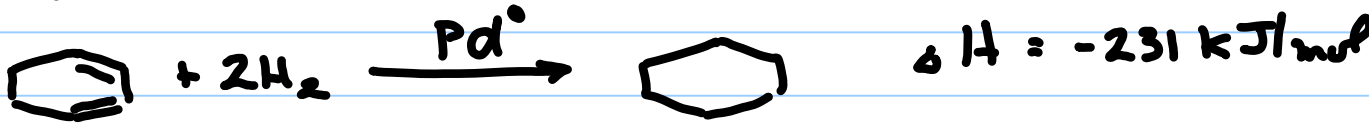
Conjugation











$\Delta H_{PREDICT} \approx -360\ kJ/mol$

$\Delta H_{ACTUAL} = -208\ kJ/mol$

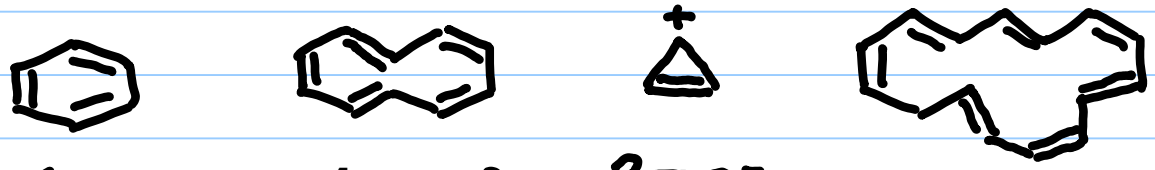
BENZENE IS 150 kJ/mol MORE STABLE THAN 3 ISOLATED C=C's. (36 kcal/mol)

- REAL ΔH IS PROBABLY ≈ 120 kJ/mol / 28-29 kcal/mol

WORKING DEFINITION OF AROMATIC CPD.

- SYSTEM WHICH HAS STABILITY TO IT'S π-SYSTEM FAR IN EXCESS OF WHAT IS EXPECTED FROM ISOLATED π-BONDS

— WHAT COMPOUNDS DO THIS?

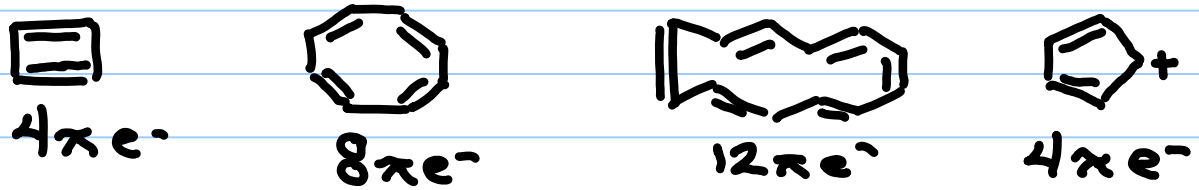


6πe⁻ 10πe⁻ 2πe⁻ 14πe⁻

CONJUGATED CYCLIC POLYENE WITH $4n+2$ π e⁻'s SHOW THIS AROMATIC STABILITY

"HUCKEL RULE" DEFINITION

how about 4? 8? 12? pi electron systems?



4πe⁻ 8πe⁻ 12πe⁻ 4πe⁻

System - Conj Cyclic Polyene with $4n$ π e⁻'s is DESTABILIZED and called Antiaromatic

(By Huckel's Rule)

How about 5π, 7π e⁻'s.

Non-Aromatic

$5\pi e^-$

$7\pi e^-$

LECTURE #2

in Karty
14.4, 14.5 MO picture of benzene, cyclobutadiene

Note Title 1/10/2017

- AROMATIC , ANTIAROMATIC , NON-AROMATIC

$4n+2\pi$ (π: pi)

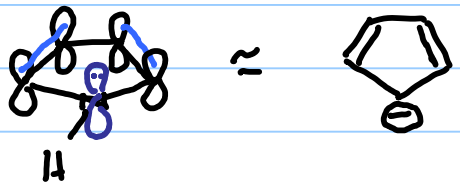
$4n$

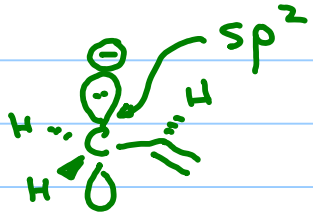
EITHER ODD #
NOT CYCLIC
NOT CONTINUOUS ARRAY OF p ORBITALS

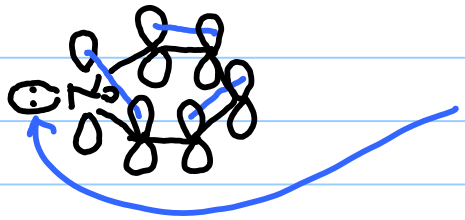
HETEROCYCLIC SYSTEMS

FURAN THIOPHENE PYRROLE PYRIDINE

- ALL AROMATIC 6 π SYSTEMS



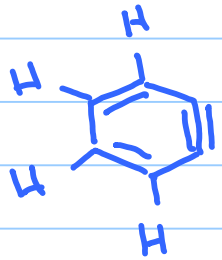




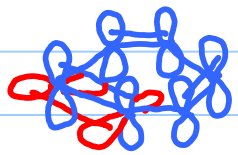
ORTHOGONAL / PERPENDICULAR TO π SYSTEM

$\therefore$ NOT INTERACTING WITH IT.

TRIPLE BONDS.



BENZYNE



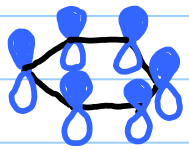
6π - ONLY ONE OF 2π BONDS OVERLAPS WITH REST OF SYSTEM

Hückel Molecular Orbital Treatment

- Consider π System Independent From the Sigma Bonds
- Create Molecular Orbitals (MO's) From Atomic Orbitals (AO's)
- Benzene - Combine 6 p Orbitals to Get 6 MO's

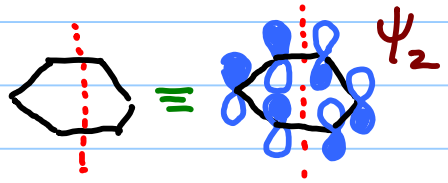
- Lowest # of Orbital Phase Changes = Lowest E & Bonding
- Highest # of Orbital Phase Changes = Highest E & Antibonding

Lowest MO



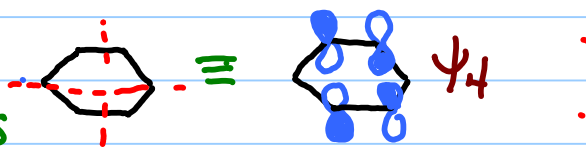
ψ_1 No Nodes

Next Lowest
1 Nodal Plane



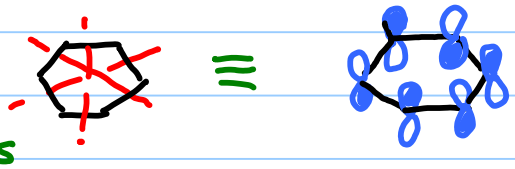
ψ_2 $\equiv$ ψ_3

2nd Highest
2 Nodal Planes

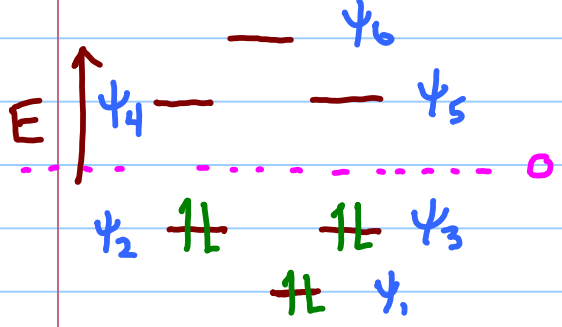


ψ_4 $\equiv$ ψ_5

Highest
3-Nodal Planes



$\equiv$ ψ_6



Everything Bonding
All e⁻'s Paired

Nice Stable Situation

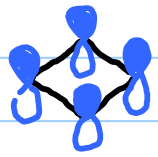
HOMO = HIGHEST OCCUPIED MOLECULAR ORBITAL

LUMO = LOWEST UNOCCUPIED M.O.

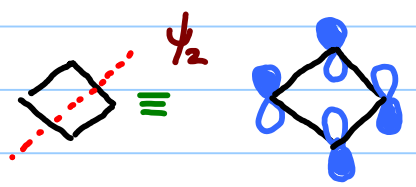
FOR. CYCLOBUTADIENE 

- 4 p ORITALS CONTRIBUTING 4 π e⁻s.

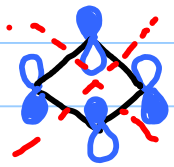
∴ 4 MO's GENERATED

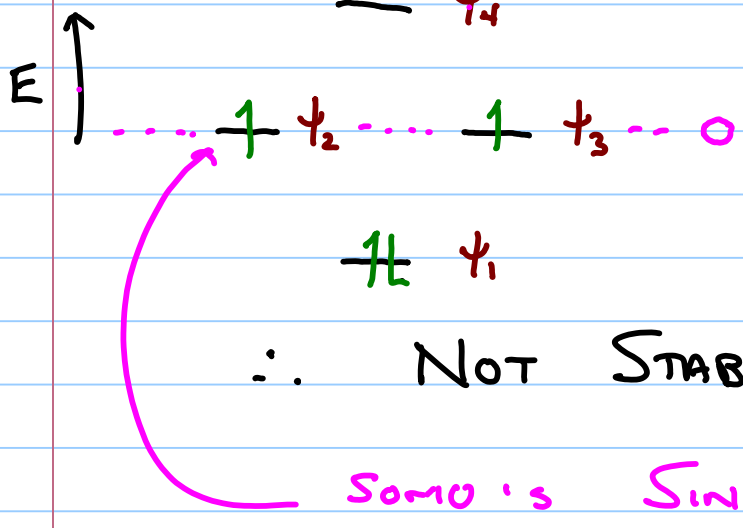
LOWEST  ψ_1

NEXT LOWEST
- 2 OF THEM
1 NODAL PLANE



HIGHEST E
- 2 NODAL PLANES

 ψ_4



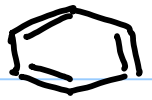
- ALL ELECTRONS ARE NOT PAIRED!
- DIRADICAL

REACTIVE LIKE CRAZY.

∴ NOT STABLE

SOMO's SINGLY OCCUPIED MO's

CONSEQUENCES IN BENZENE

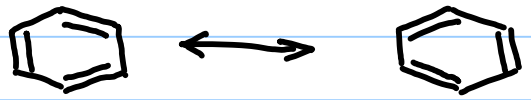


- A BIT OF A LIE
- ALL C–C BONDS SAME LENGTH

BOND LENGTH 1.398 A°

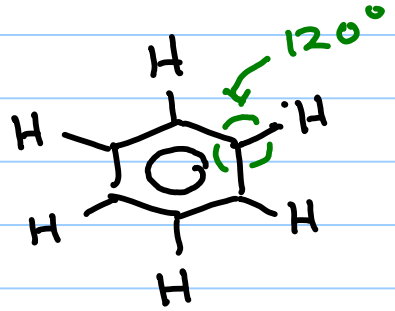
C=C BOND ORDER 1.5

(C–C ≈ 1.53 A° C=C ≈ 1.32 A°)



COULD DRAW AS

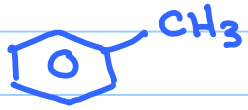
 OR  VERY COMMON SHORTHAND



- ALL BOND ANGLES = 120°
- ALL C ATOMS ARE sp^2
- ABSOLUTELY PLANAR

∴ "NO" STEREOCHEMISTRY TO ADDRESS

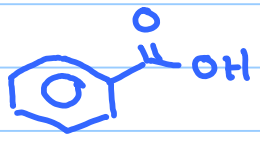
LOTS OF TRIVIAL NAMES



TOLUENE

PHENOL

ANILINE



BENZOIC ACID

NAPHTHALENE

Lecture 3

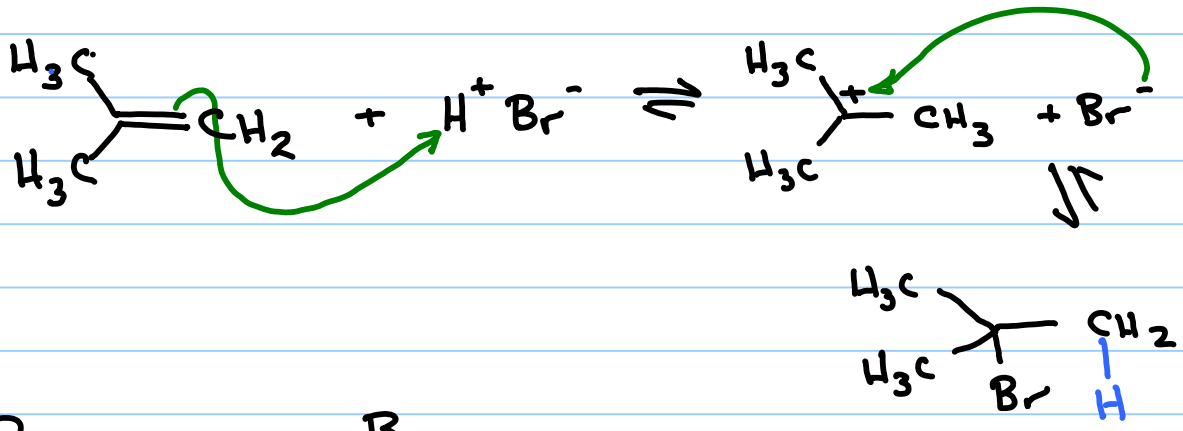
Note Title

in Karty
22.1 General Mech of Electrophilic Aromatic Subst.
22.2 Halogenation
22.3 Friedel-Crafts Alkylation
22.6 Nitration

1/12/2017

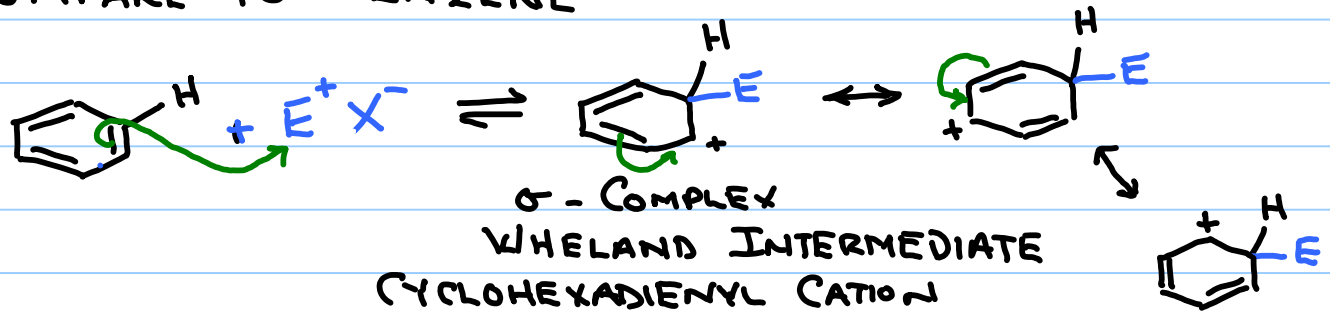
Reactions of Benzenes

Review – Electrophilic Addn. to Alkenes



Compare to Benzene

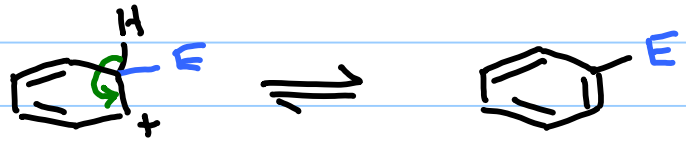
Step 1



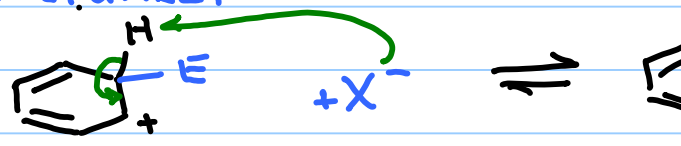
σ-Complex
Wheland Intermediate
Cyclohexadienyl Cation

- Cation has lost 120 (150?) kJ/mol of aromatic stabilization.
- Gets aromatic stabilization back by losing H^+ (from carbon that did attack)

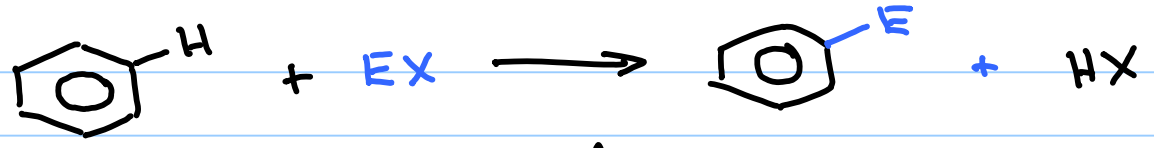
Step 2



Actually



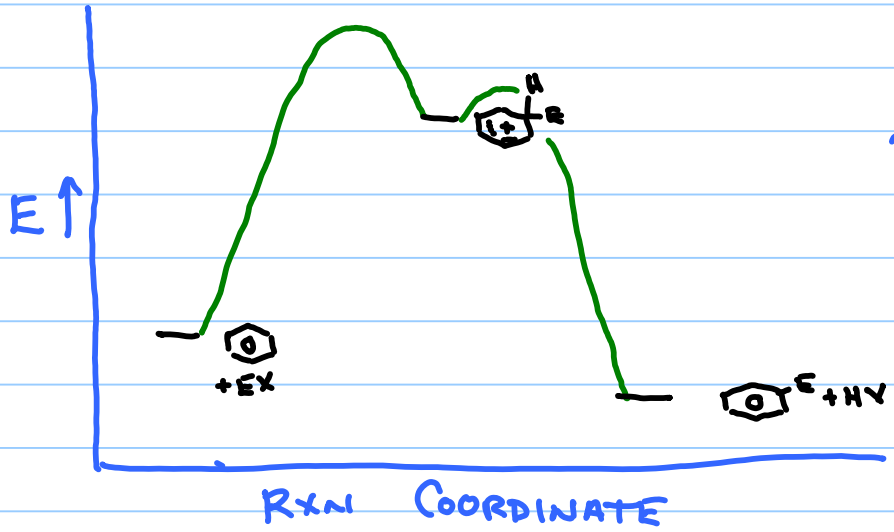
OVERALL



CALLED ELECTROPHILIC AROMATIC SUBSTITUTION

S_E2

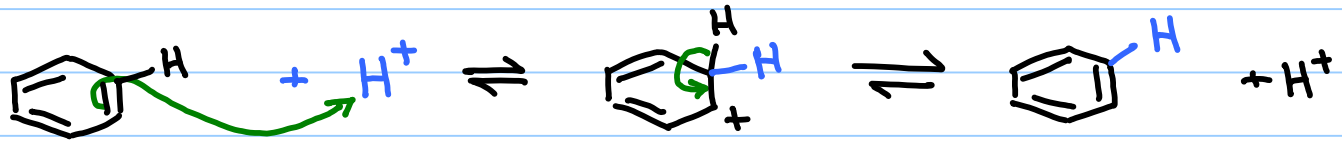
2 STEPS ; 1ST ONE IS RATE DETERMINING (SLOW)



$v = k[\text{C}_6\text{H}_6][EX]$

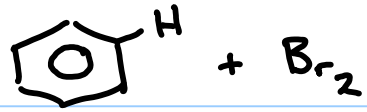
THE FIVE/SIX MAIN EXAMPLES

1) PROTONATION $E^+ = H^+$

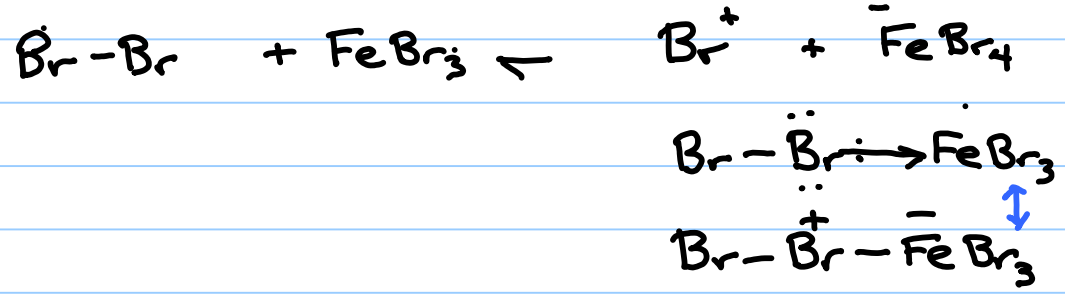


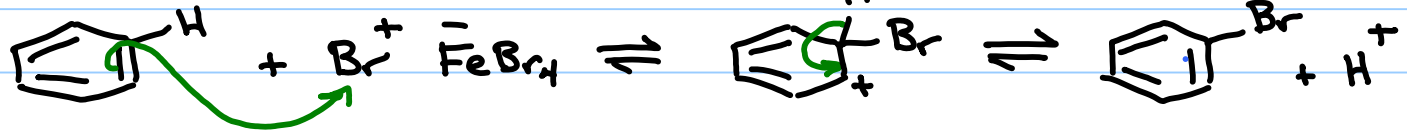
- USUALLY INVISIBLE RXN
- BUT CAN BE USED TO DEUTERATE BENZENE, OR DO OTHER USEFUL THINGS

2) HALOGENATION $E^+ = Br^+, Cl^+$

 + Br_2 ⟶ JUST SITS THERE

BUT, ADD A LEWIS ACID $FeBr_3$



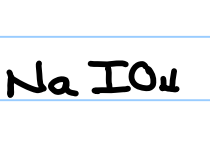


OVERALL

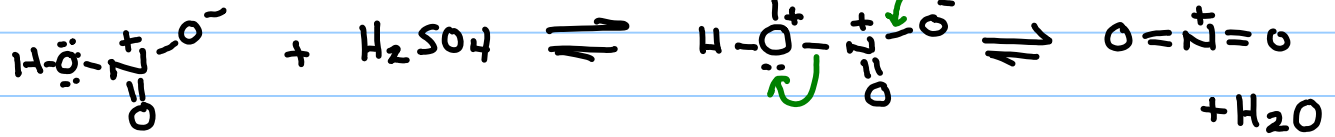
FOR CHLORINATION

FLUORINATION ? – NO F_2 JUST TOO REACTIVE

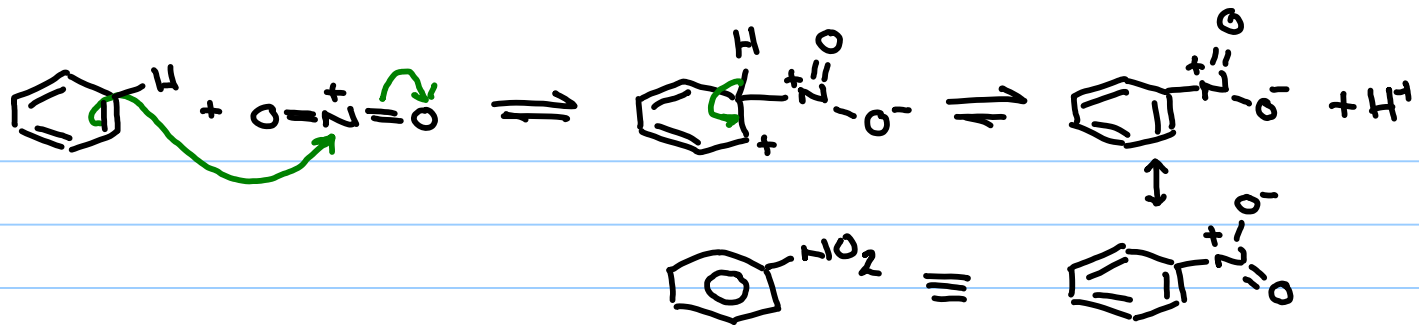
IODINATION ? – NOT REALLY TOO UNREACTIVE

RECENT PROGRESS $I_2 + NaIO_4 \xrightarrow{H_2SO_4}$ 

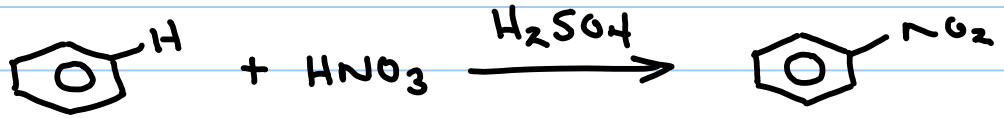
3) NITRATION $E^+ = \overset{+}{N}O_2$ ($O{=}\overset{+}{N}{=}O$)



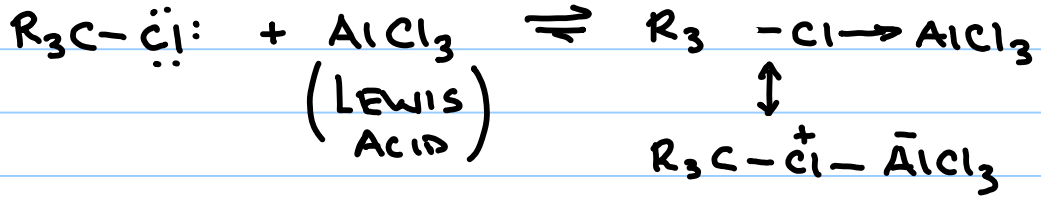
(HNO_3) (H^+)



OVERALL



4) FRIEDEL-CRAFTS ALKYLATION $E^+ = \overset{+}{C}R_3$



IF R_3C-X IS

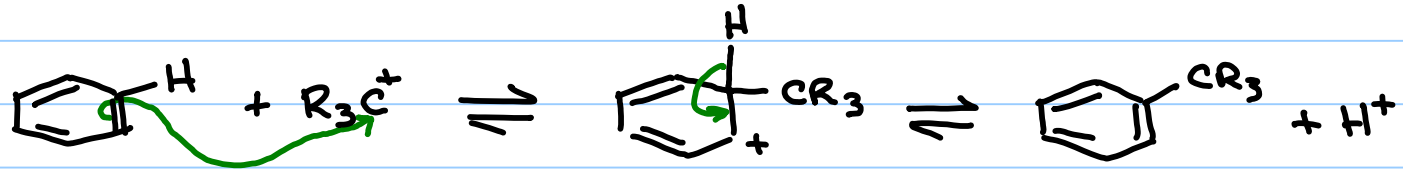
CH_3 OR 1°

COMPLEX IS TRUE STRUCTURE

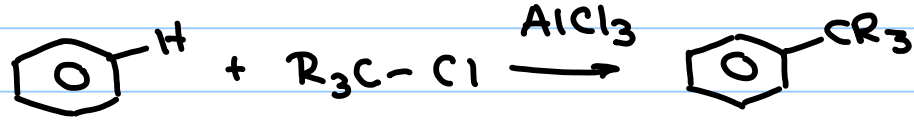
IF R_3C-X IS

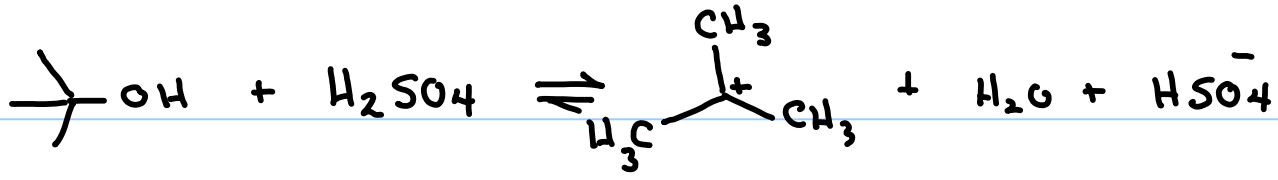
2° OR 3°

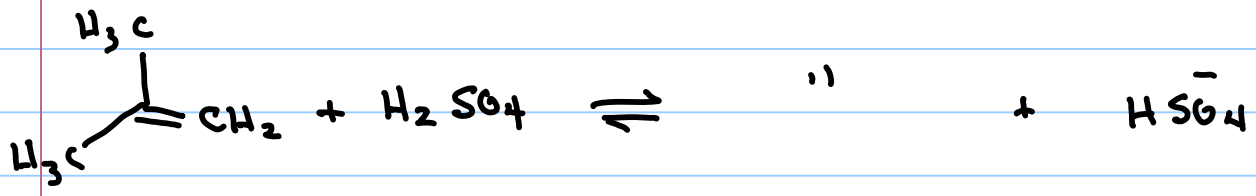
ION PAIR IS TRUE STRUCTURE



OVERALL







FOR PUTTING IN A " $\overset{+}{C}H_3$ ", USE H_3C-I

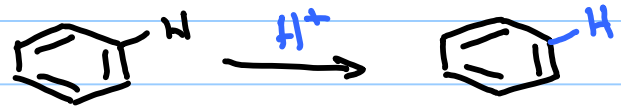
- ONLY CH_3-X THAT ISN'T A GAS

Lecture 4

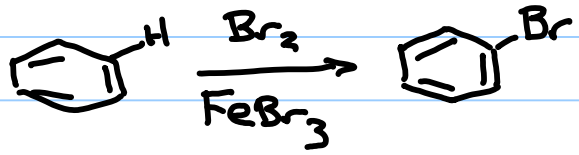
in Karty
22.5 Friedel-Crafts Alkylation
22.7 Sulfonation

Note Title 1/17/2017

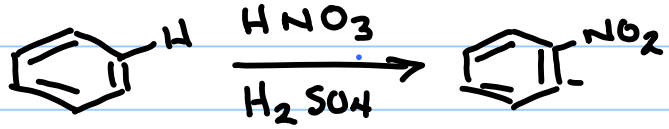
To do a Quick Review



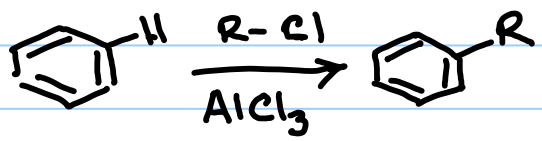
Protonation



Halogenation



Nitration

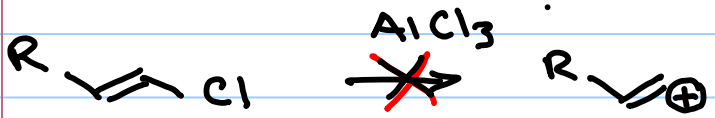


Friedel-Crafts Alkylation

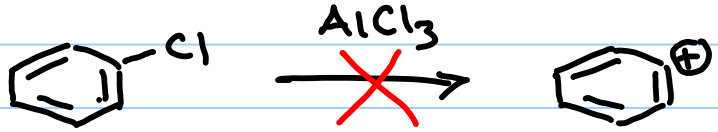
Note:

3°, OK 2°, OK 1°, OK often Methyl, OK

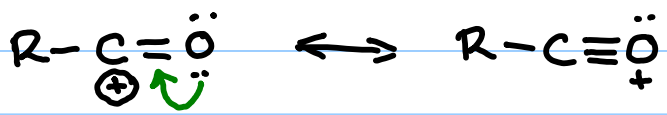
But not.....



Doesn't work Too unstable

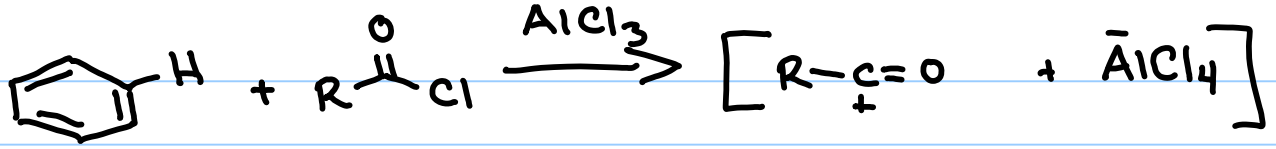


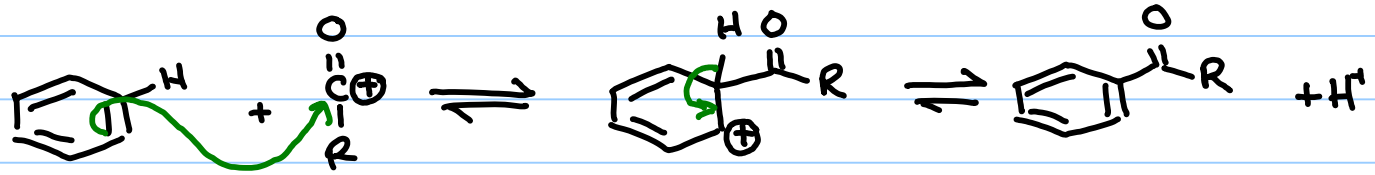
No.... to unstable

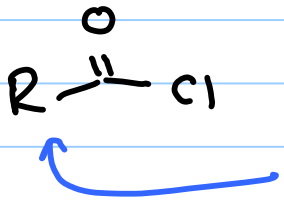
5) 

Friedel-Crafts Acylation

Acylium Ion



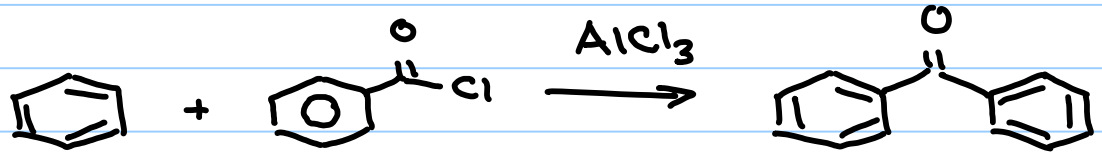




CAN BE MANY THINGS.

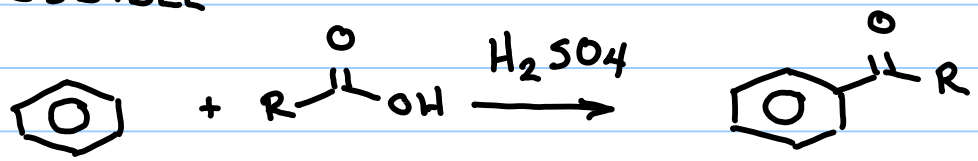
ALKYL, ARYL, ETC.

NOT H

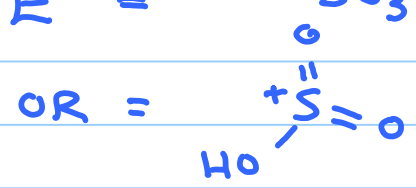


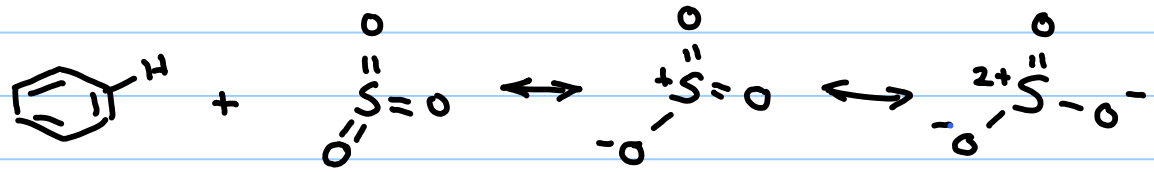
NOTE:

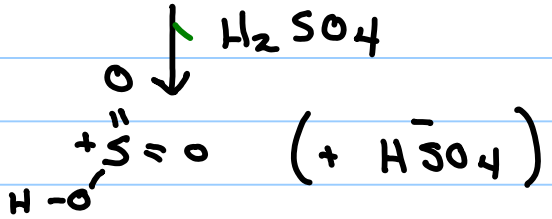
ALSO POSSIBLE

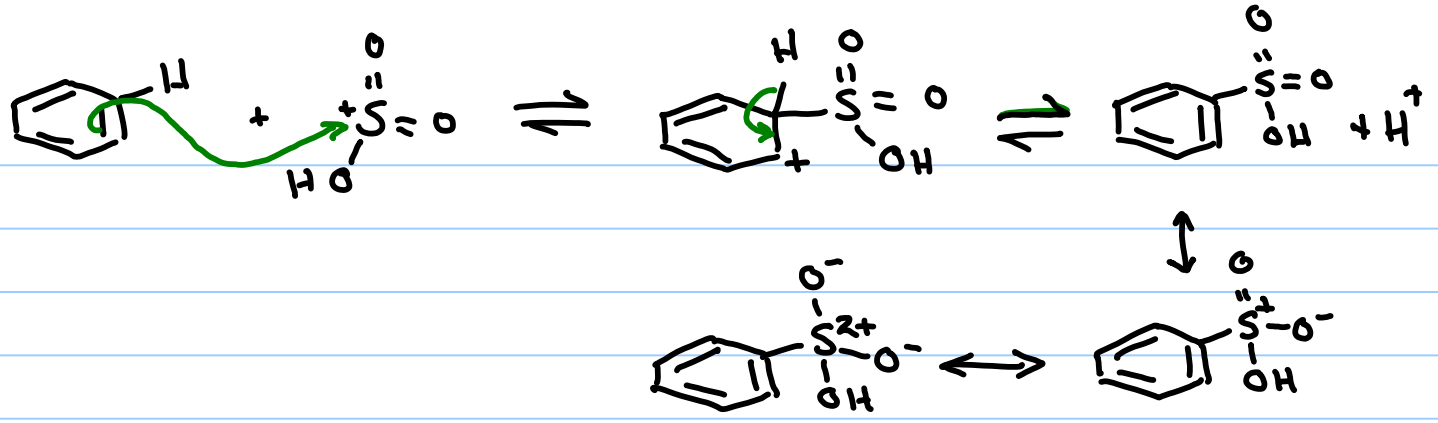


6) SULFONATION

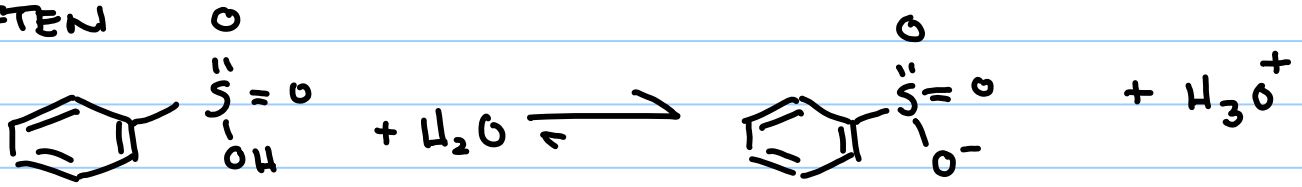
$E^+ =$ 



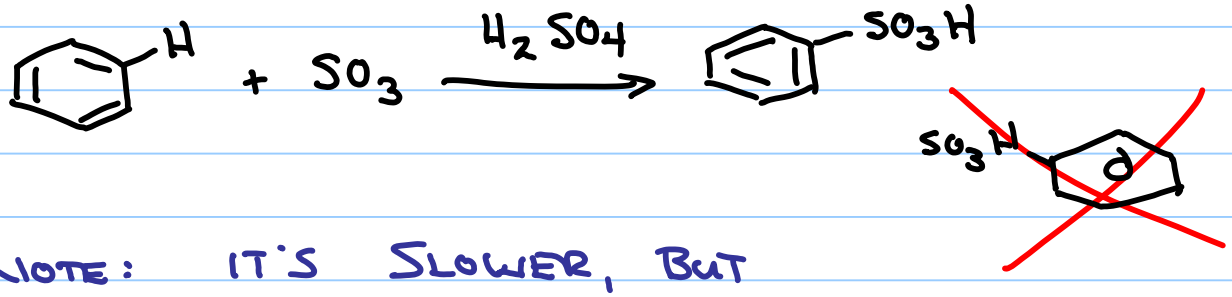




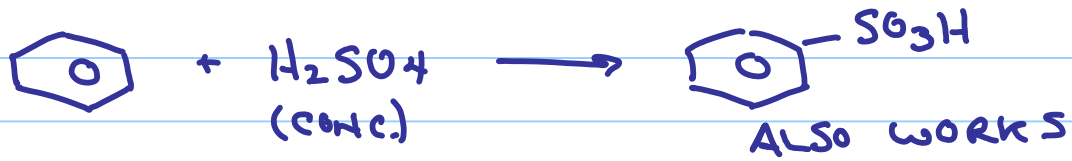
OFTEN



OVERALL



NOTE: IT'S SLOWER, BUT

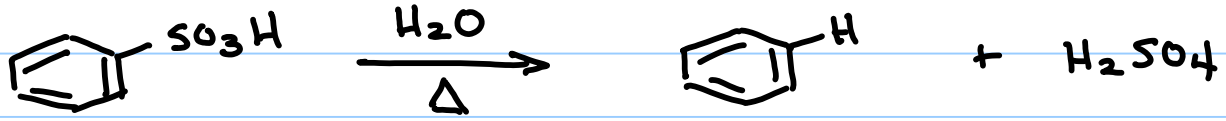


ALSO WORKS

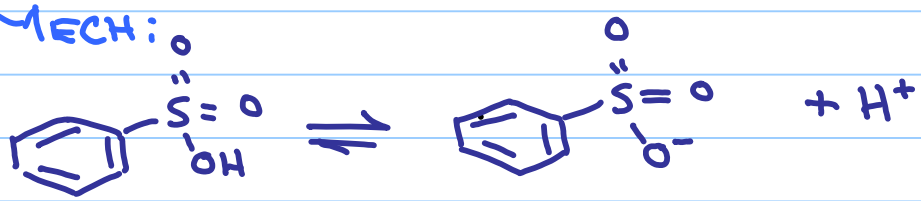
NOTABLE DIFFERENCE OF SULFONATION —

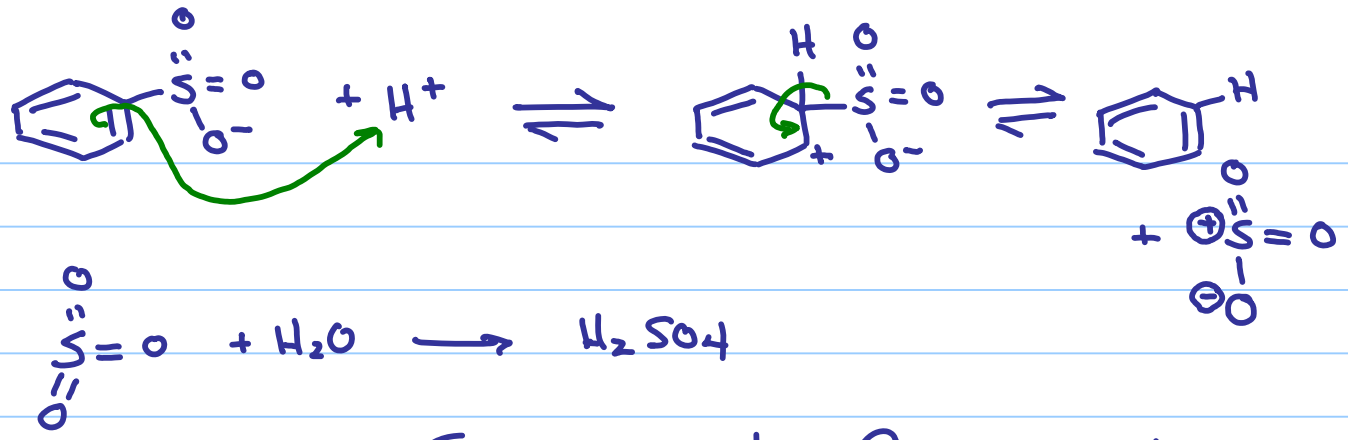
IT CAN BE REVERSED

(dil. H_2SO_4 IN PRACTICE)



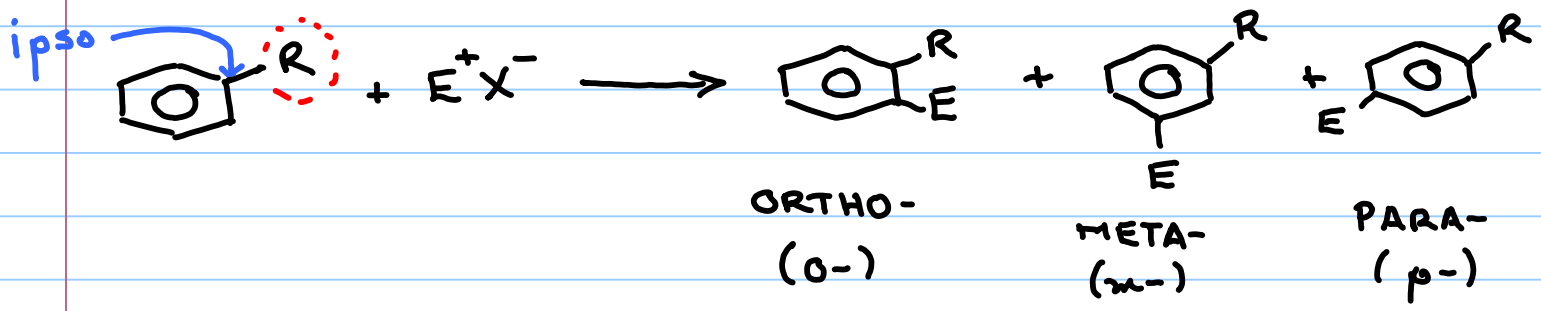
MECH:





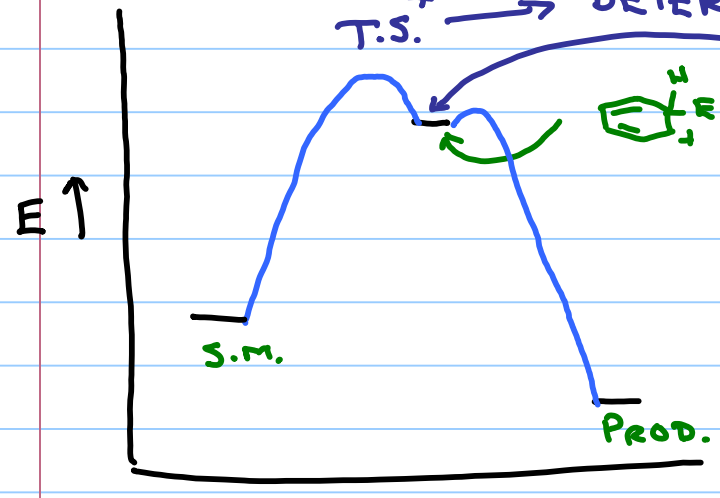
DESTROYED - SO IT'S A LE CHATELIER'S PRINCIPLE "TRICK"

WHAT HAPPENS WITH A SUBSTITUTED BENZENE?



- WHICH YOU GET DEPENDS ON THAT EXISTING R-

- NEVER STATISTICAL (2:2:1 o- : m- : p-)



WE'LL USE CLOSEST THING IN ENERGY TO APPROXIMATE T.S.‡ STRUCTURE (HAMMOND POSTULATE)

TWO POSSIBILITIES FOR 

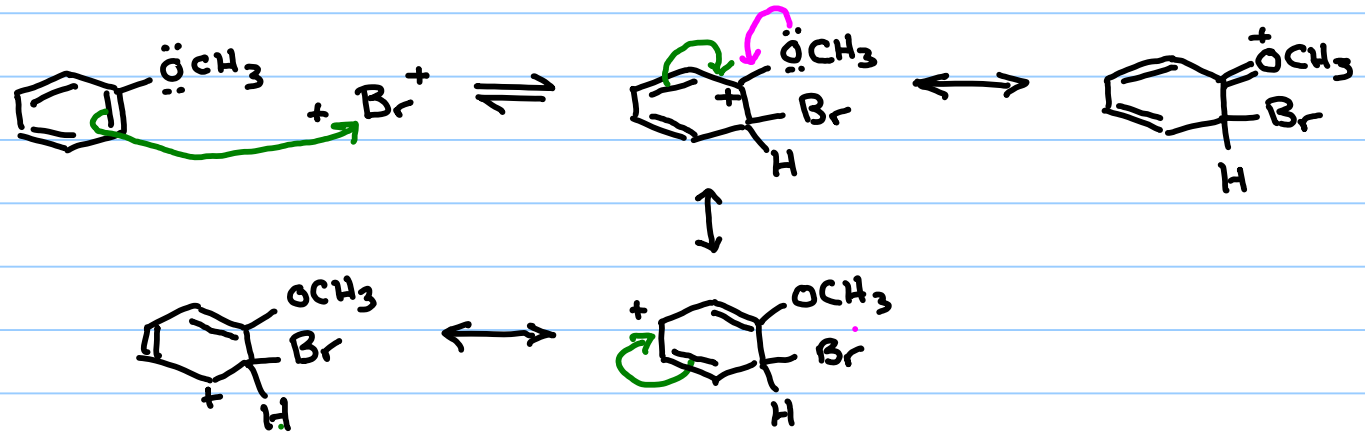
R = EDG (ELECTRON DONATING GROUP, BY RESONANCE (+M) OR INDUCTIVE EFFECTS (+I))

R = EWG (ELECTRON WITHDRAWING GROUP -M OR -I)

i) DONATING EDG.

- ALKYL OR ARYL GROUPS (+I)
- GROUPS W/ LONE PAIRS ON ATOMS IMMEDIATELY ADJACENT TO BENZENE – $\ddot{O}CH_3$

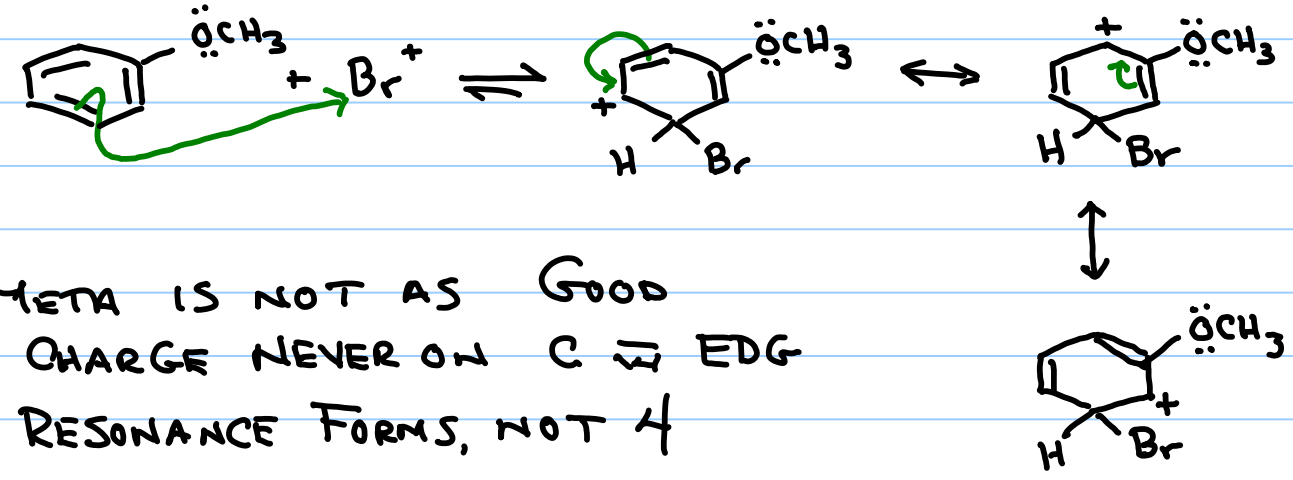
o-



- THIS IS GOOD + CHARGE ON C ATOM BEARING EDG
  4 GOOD RESONANCE FORMS

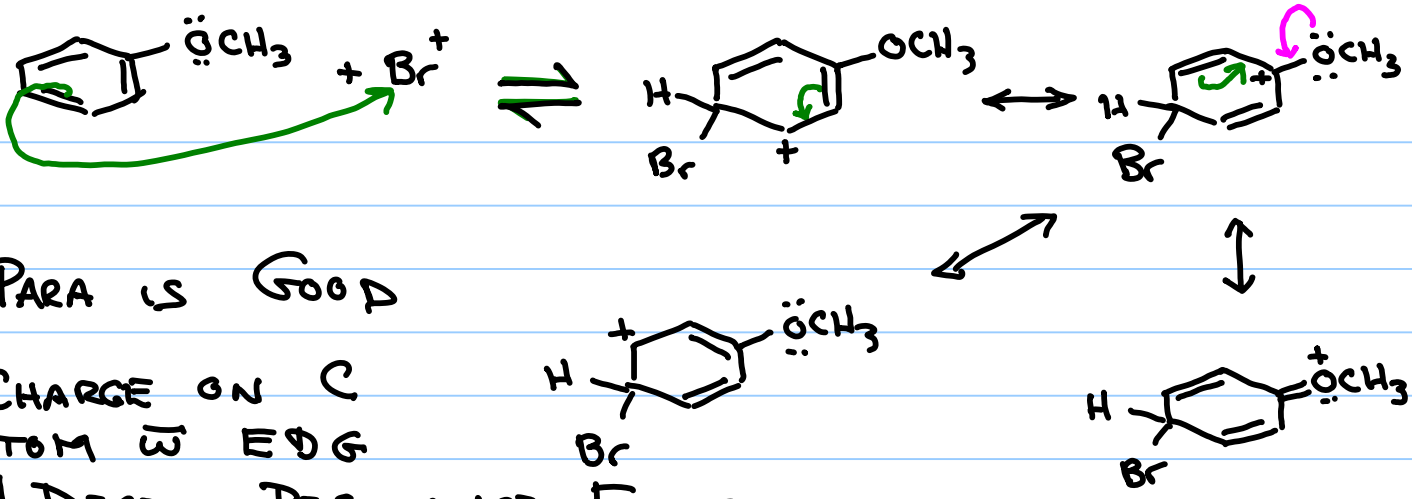
---

m-



META IS NOT AS GOOD
+ CHARGE NEVER ON C W/ EDG
3 RESONANCE FORMS, NOT 4

p-



∴ PARA IS GOOD

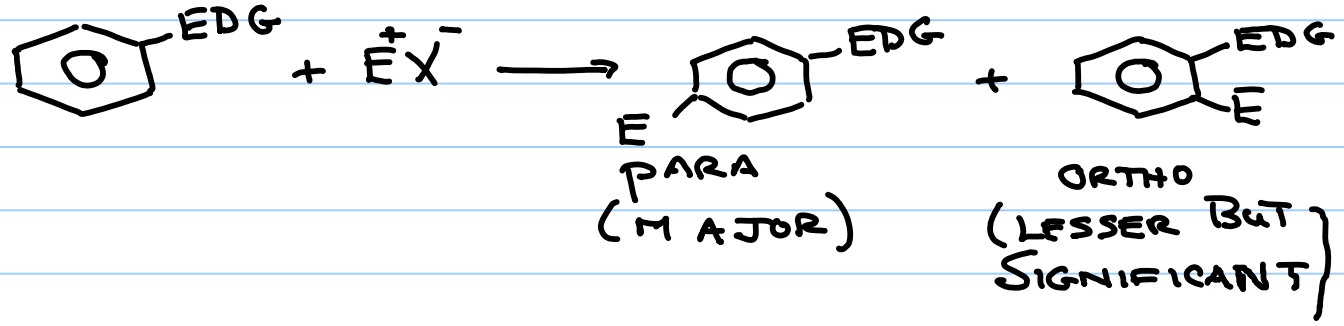
+ CHARGE ON C ATOM W EDG

- 4 DECENT RESONANCE FORMS

TAKE HOME MESSAGE

- WILL BE MORE REACTNE THAN BENZENE (ACTINATED)

-

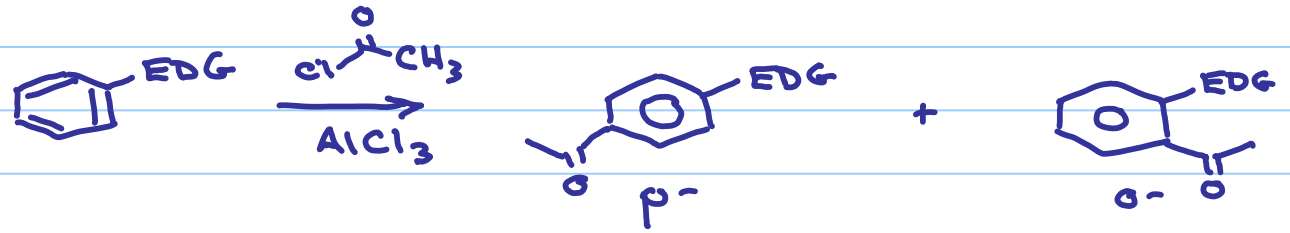


LECTURE # 5

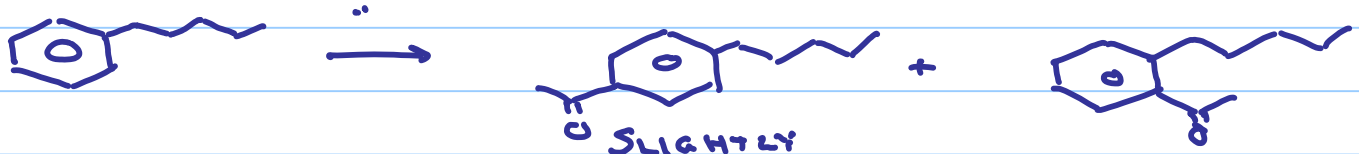
Corresponding sections from Karty
Activating/deactivating/o-,p- and m-directors 23.1-23.5
Disubstituted cases 23.5

Note Title 1/19/2017

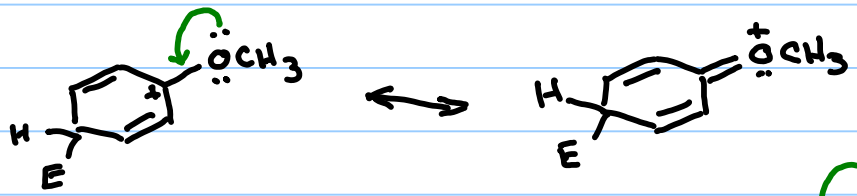
EDG'S. IN ELECTROPHILIC AROMATIC SUBST.

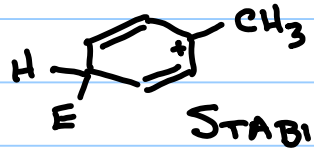


MAJ MIN.

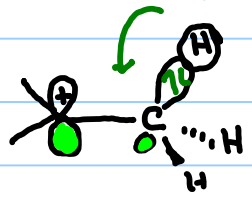


REASONS





STABILIZED BY HYPERCONJUGATION



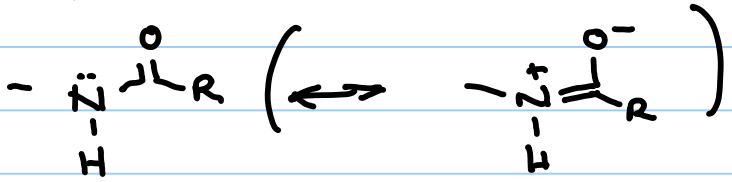
FILLED σ ORBITAL CAN DONATE e^- DENSITY TO EMPTY p- ORBITAL

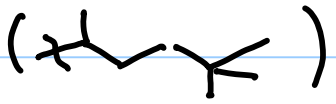
TYPICAL EDG'S

STRONG $-\ddot{N}(R)(R)$ $(-\ddot{N}H_2)$

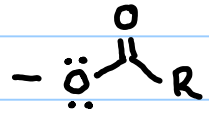
$-\ddot{O}H$

MEDIUM $-\ddot{O}R$ (i.e., $-OCH_3$)



WEAK - alkyl 

- PHENYL 

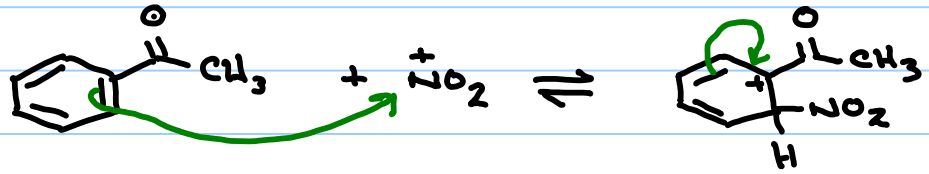


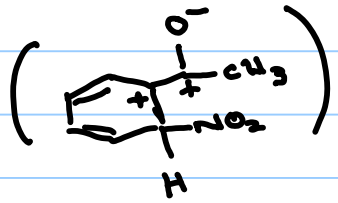
LOOK FOR

E·WG (ELECTRON WITHDRAWING GROUPS)

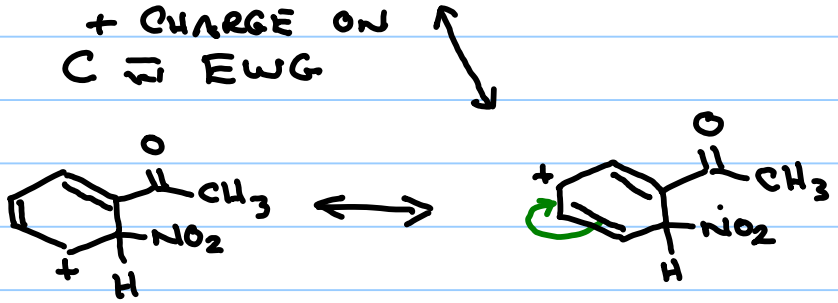
- RXN IS SLOWER THAN BENZENE

ORTHO



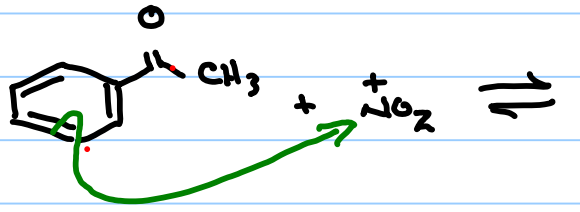


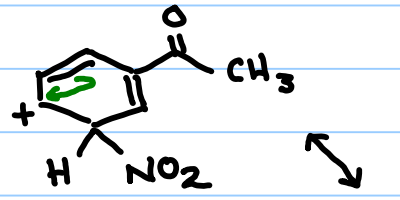
BAD - + CHARGE ON C $\overline{\text{W}}$ EWG

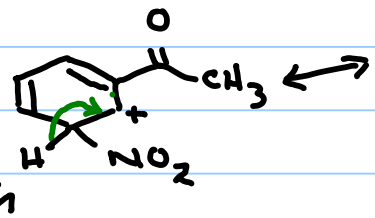


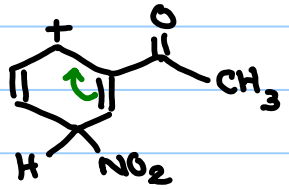
NOT LIKELY. DISFAVOURED

META



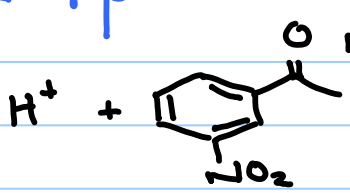




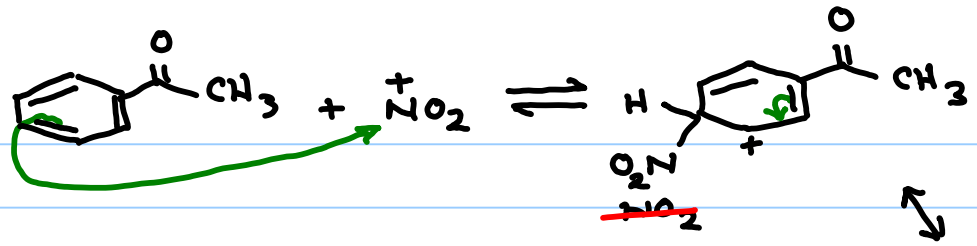


NEVER PUT + CHARGE ON C $\overline{\text{W}}$ EWG

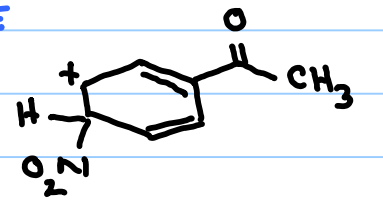
∴ BEATS O⁻ +P⁻

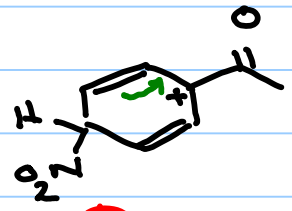


PARA-



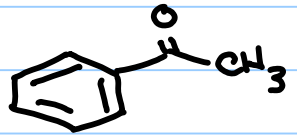
DISFAVOURED, SINCE + CHARGE IS ON C W EWG



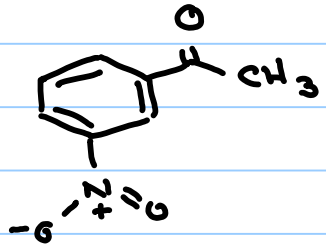


BAD

OVERALL



HNO_3 / H_2SO_4



META WINS BY DEFAULT

TYPICAL EWG / DEACTIVATING m- DIRECTORS

STRONG $-NO_2$ $\left(-\overset{+}{N}\overset{O}{\overset{\|}{}}\overset{-}{O}\right)$

$-\overset{+}{N}R_3$ $(-\overset{+}{N}H_3)$

MEDIUM $-C\equiv N$

$-CF_3$

$-\overset{O}{\overset{\|}{C}}-CH_3$, $-\overset{O}{\overset{\|}{C}}-H$, $-\overset{O}{\overset{\|}{C}}-H$, $-\overset{O}{\overset{\|}{C}}-OR$, $-\overset{O}{\overset{\|}{C}}-NR_2$

$-SO_3R$, $-SO_3H$

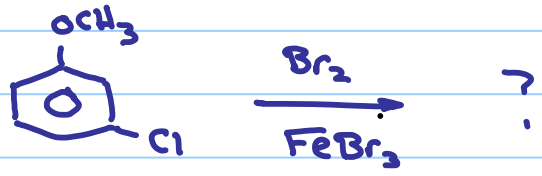
NOTE: 2ND ATOM FROM BENZENE USUALLY MORE EN THAN 1ST ATOM.

THE HALOGENS $-\ddot{F}:$ $-\ddot{Cl}:$ $-\ddot{Br}:$, $-\ddot{I}:$

- TWO FEATURES
  - THEY'RE ELECTRONEGATIVE (INDUCTIVELY ELECTRON WITHDRAWING) (−I)
  - THEY'RE (+M) — :X: RESONANCE DONATING
  - BUT ONLY WEAKLY.

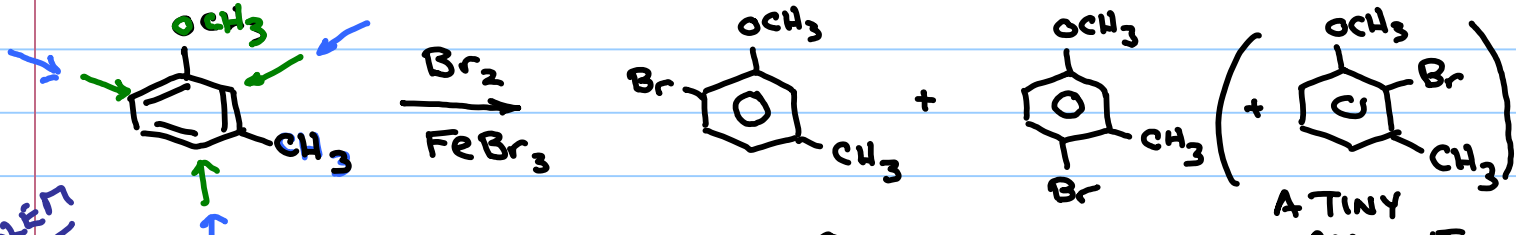
OVERALL - ORTHO, PARA - DIRECTING, BUT SLIGHTLY DEACTIVING (10% OF RATE OF BENZENE)

DISUBSTITUTED BENZENES.

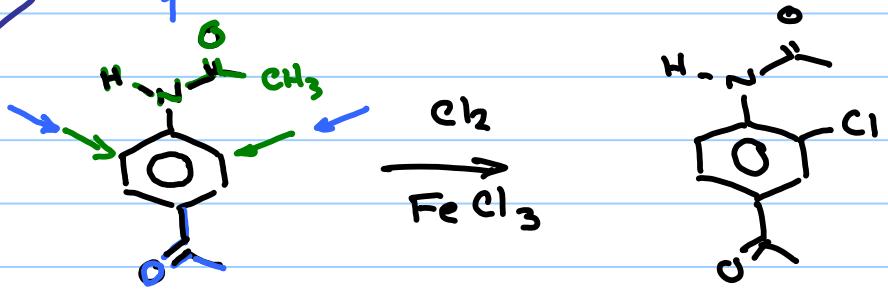


- DEPENDS ON SITUATION.

1) IF TWO GROUPS ARE TRYING TO DO THE SAME THING.

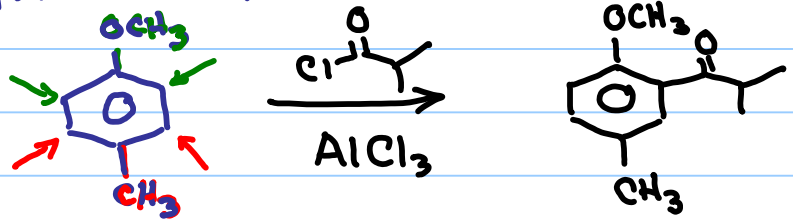


NO PROBLEM

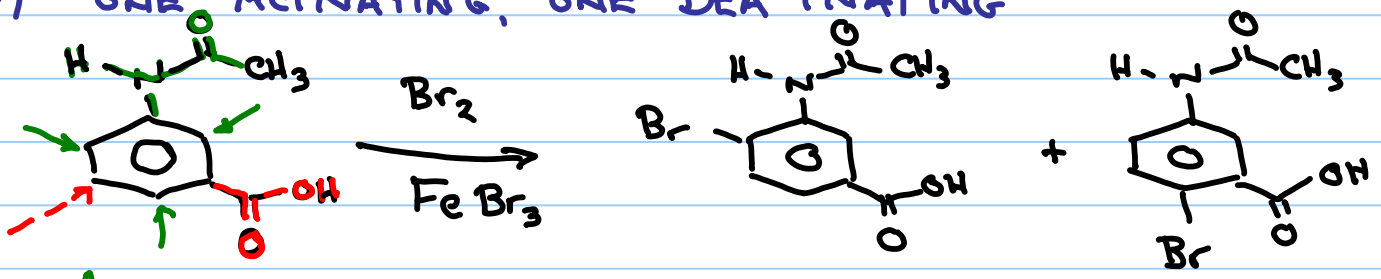


---

2. a) IF THEY DISAGREE - STRONGER ACTIVATOR WINS

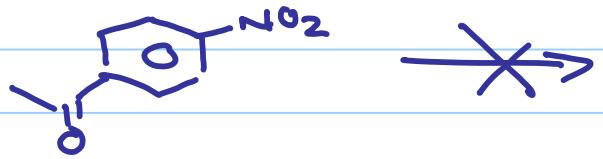


b) ONE ACTIVATING, ONE DEACTIVATING



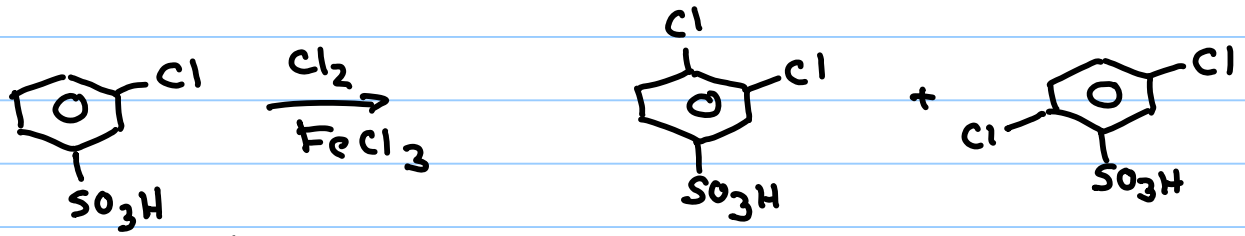
ACTIVATING GROUP WINS

c) TWO DEACTIVATING GROUPS



FORGET IT
TOO DEACTIV-TING

EXCEPTION - HALOGENS



HALOGEN WINS

SIDE CHAIN REACTIONS

- OXIDATIONS OR REDUCTIONS
- LOSS OF H ATOMS — ADDN OF H ATOMS
- ADDN OF 'O' ATOMS — LOSS OF 'O' ATOMS

LECTURE #6

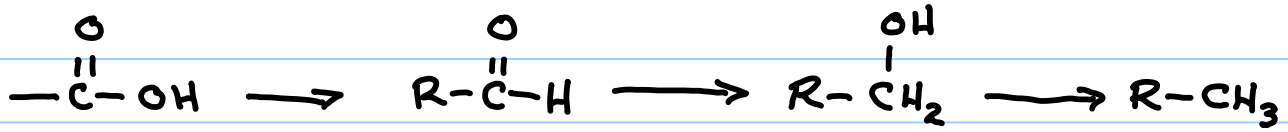
Note Title 1/24/2017

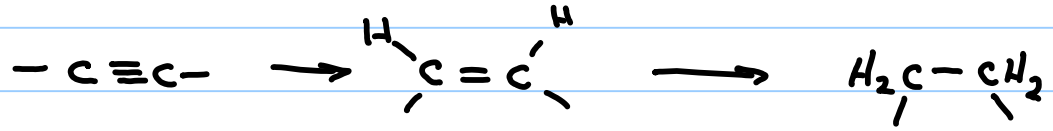
Corresponding sections in Karty
22.4 F/C alkylation problems 22.8 Acylation/reduction
22.9a,b Side chain rxns
23.12 Attaching groups in right order

SIDE CHAIN FUNCTIONALIZATION RXNS

ORGANIC DEFINITION - REDUCTION

- ADDN OF H ATOMS, LOSS OF O ATOMS

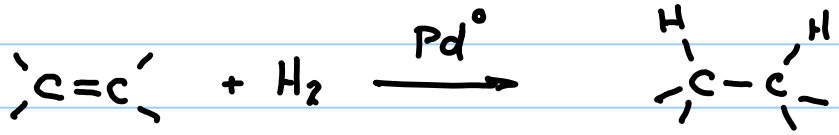




OXIDATION - REVERSE -

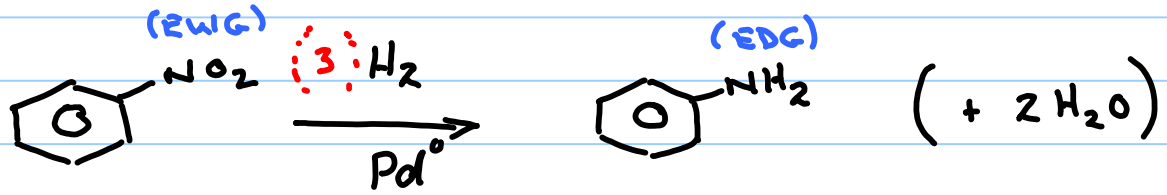
ADDN OF O ATOMS, OR LOSS OF H ATOMS

1) REDUCTION OF NITRO GROUPS

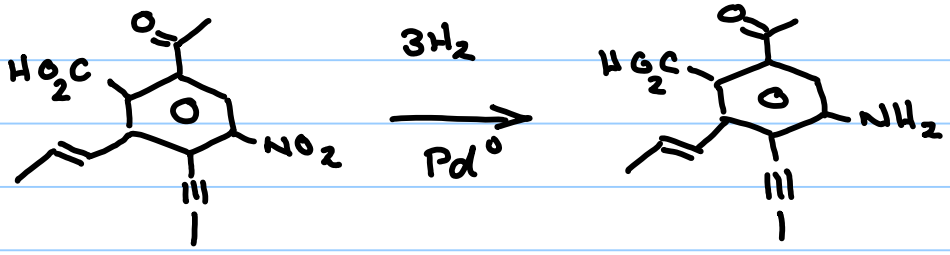


Note: Treatment with H2 and catalyst is very common way to reduce alkenes

EVEN EASIER THAN ALKENE REDUCTION IS...



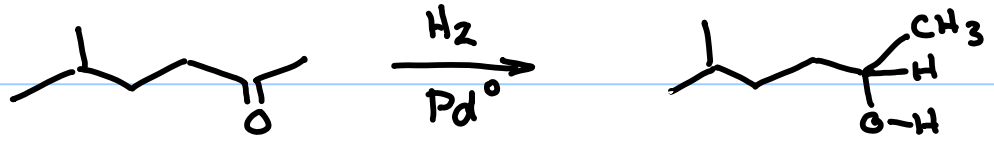
V. EASY



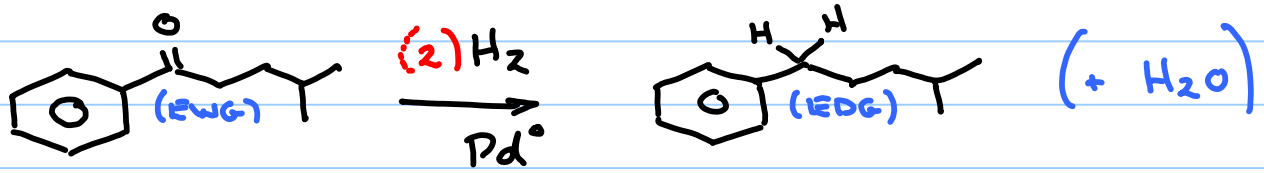
nitro groups are reduced more readily than almost *anything* else

2. REDUCTIONS OF ARYL KETONES / ALDEHYDES

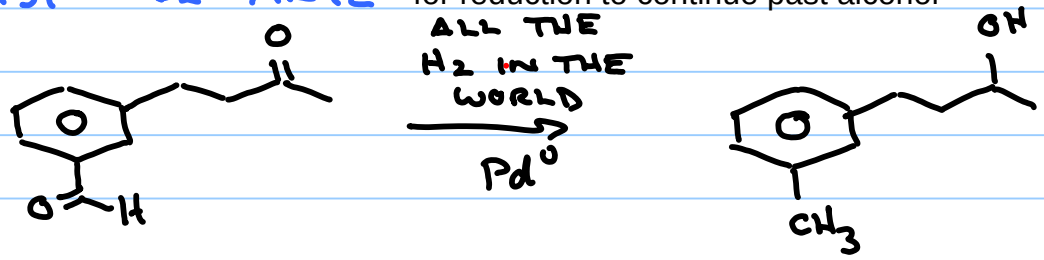
TYPICAL ALDEHYDE / KETONE



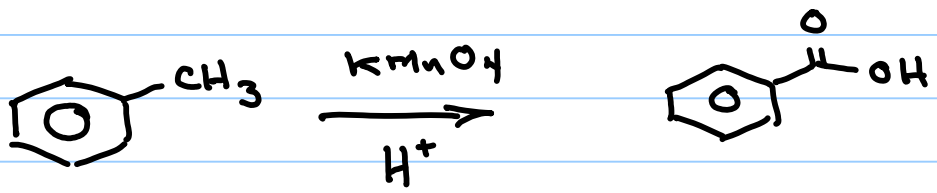
IF IT'S AN ARYL KETONE / ALDEHYDE



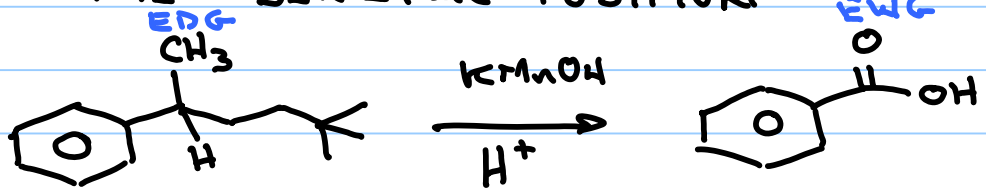
MUST BE ARYL for reduction to continue past alcohol

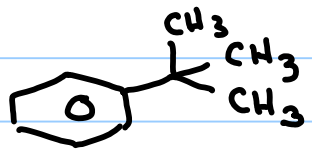


3) OXIDATION OF ALKYLBENZENES BY $KMnO_4$



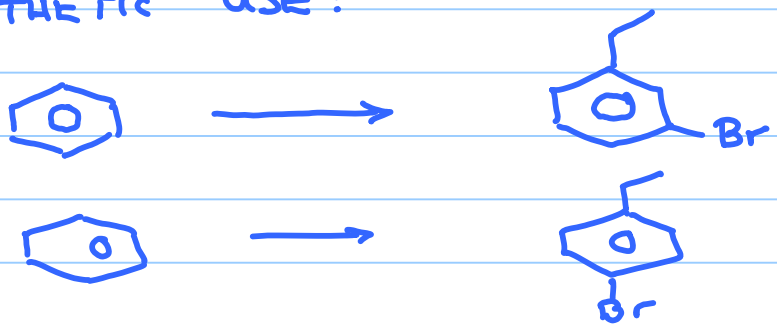
IN FACT, ANY ALKYLBENZENE THAT HAS. $\geq$ H IN THE BENZYLIC POSITION



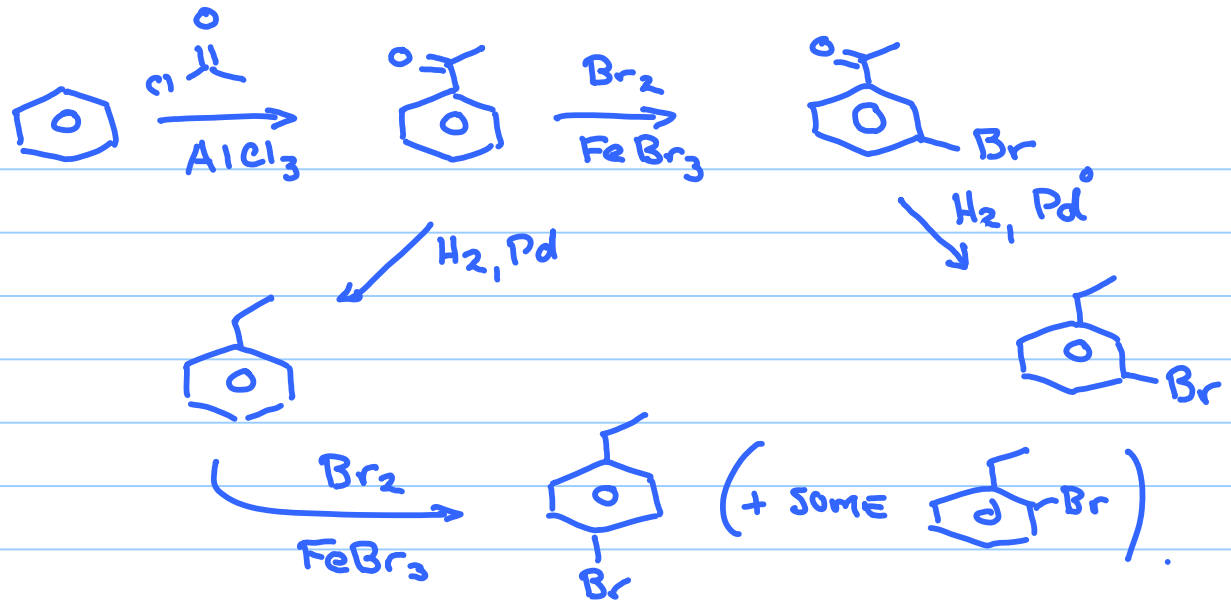


INERT

SYNTHETIC USE:



a)

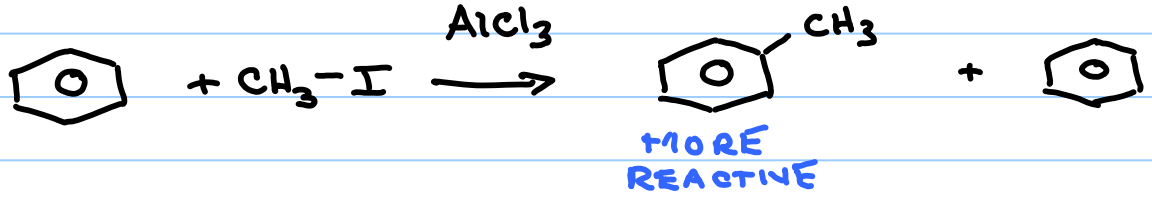


so timing of reactions is sometimes *as* important as the reactions themselves

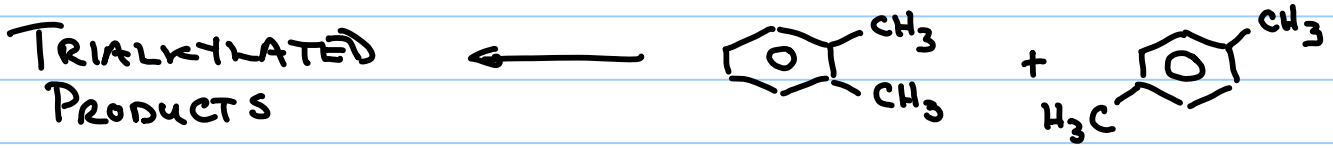
PROBLEMS W FRIEDEL CRAFTS ALKYLATIONS

i) POLYALKYLATION

AT 50% CONVERSION



MORE REACTIVE

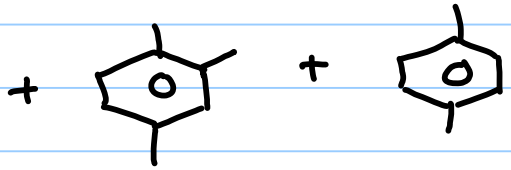


TRIALKYLATED PRODUCTS

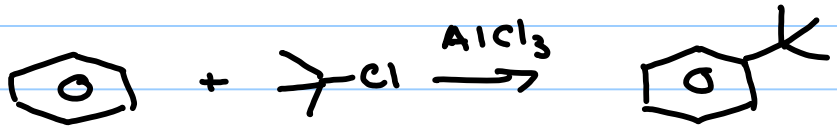
NOW EVEN MORE REACTIVE

1 mol 1 mol

OTHERS



NOT ALWAYS DEADLY



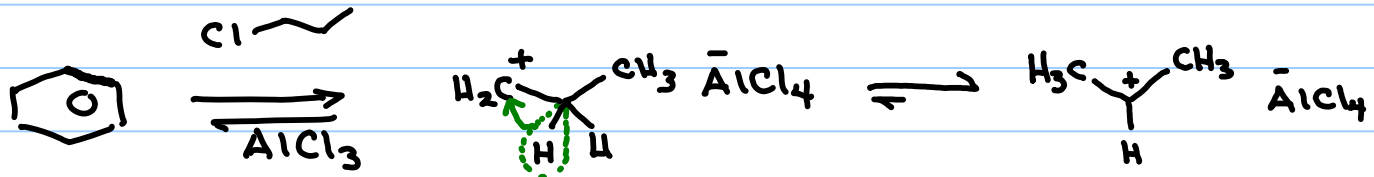
XS

DECENT RESULT

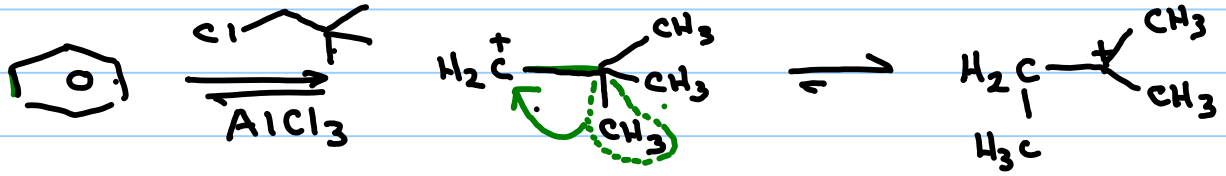
SINCE ALKYL GROUPS ACTIVATE BY A MODEST AMOUNT.

so you can often overwhelm the polyalkylation problem with excess (xs) starting arene

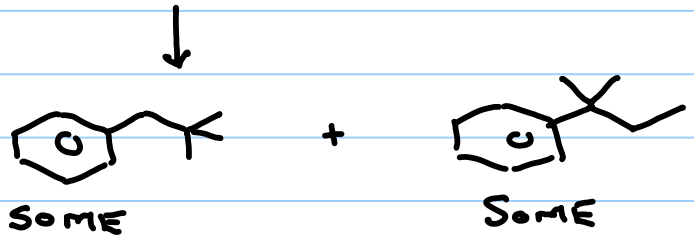
2) Carbocation Rearrangements



1° Cation 2° Cation

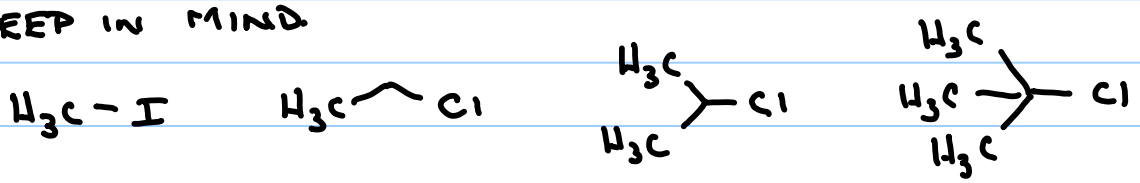


1° 3°



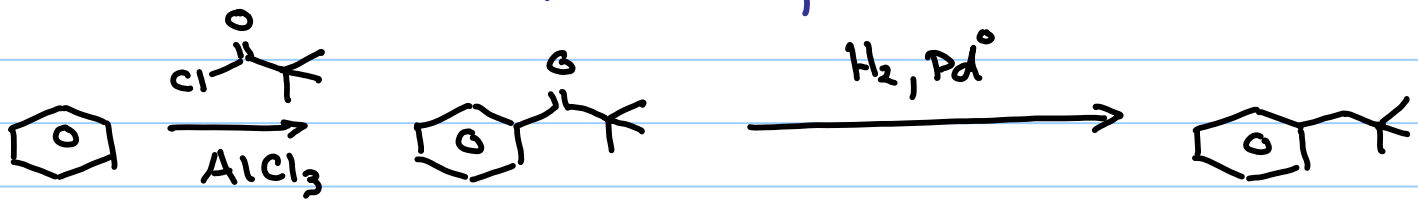
some some

Keep in mind



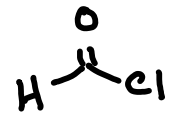
are not problems

Solution: F/C Acylation, then Reduction



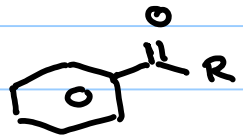
no Polyacylation
no Rearr.

- Very often better to do Acylation, then Reduction, than Alkylation

DRAWBACKS i)  NOT A STABLE CPD.

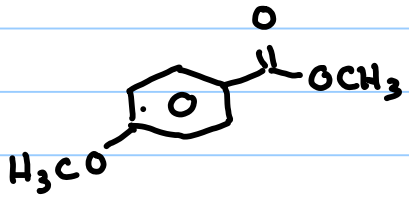
ii) FRIEDEL CRAFTS ACYLATIONS / ALKYLATIONS DON'T WORK ON BENZENES W MEDIUM OR STRONGER EWG'S.

OK

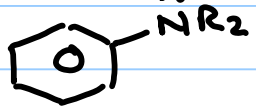


NOT REACTIVE

NOT REACTIVE

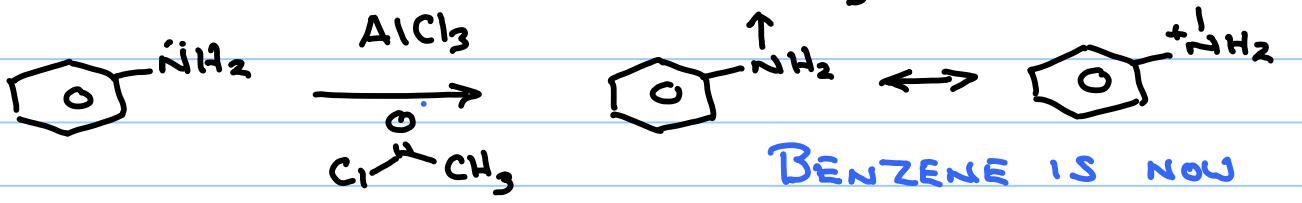


O.K, BECAUSE HAS ACTIVATING GROUP TOO.



ALSO UNREACTIVE TO FRIEDEL-CRAFTS.

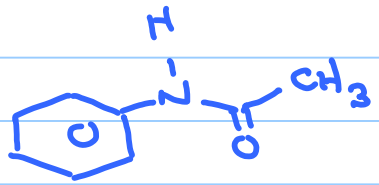
LONE PAIR MAKE AMINE LEWIS BASIC (AND BRONSTEAD BASIC)



BENZENE IS NOW STRONGLY DE-ACTIVATED

≡ 

SOLUTION

GO TO 

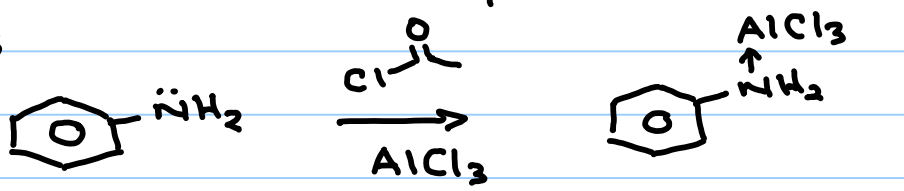
IN KARTY 23.13 AMIDE P.G.'S
25.4 BENZYLIC BROMIN.
22.9c DIAZONIUM SALTS

LECTURE 7

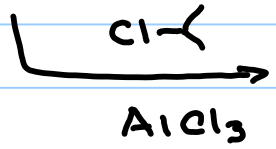
Note Title 1/26/2017

- MIDTERM #1 FEB 9TH 10-11 AM.
  50% HERE, 50% 1120 ERIE

TUES

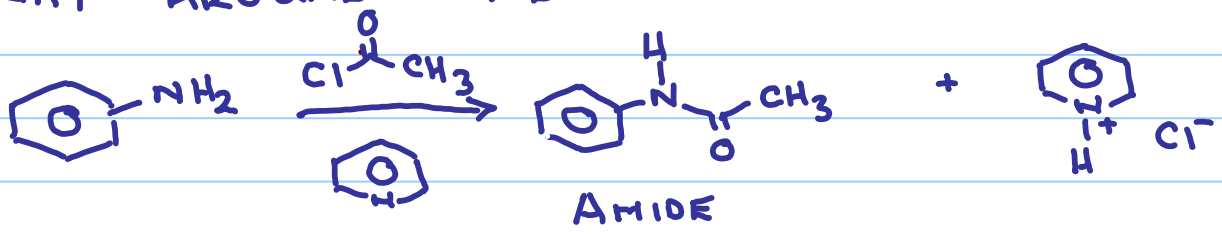


NOW DEAD TO FRIEDEL-CRAFTS



same problem

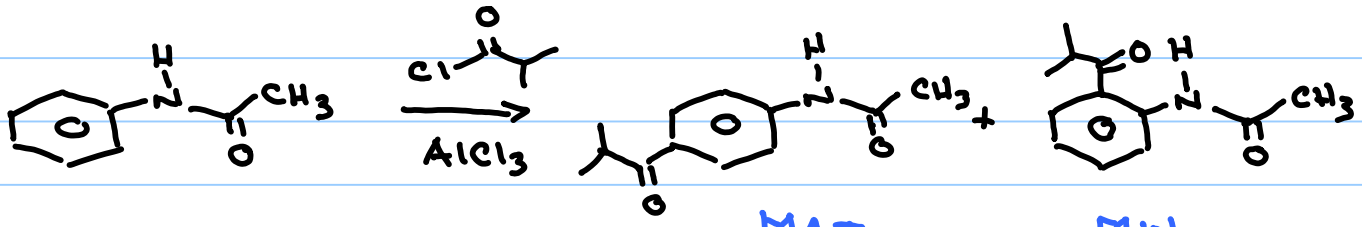
WAY AROUND THIS



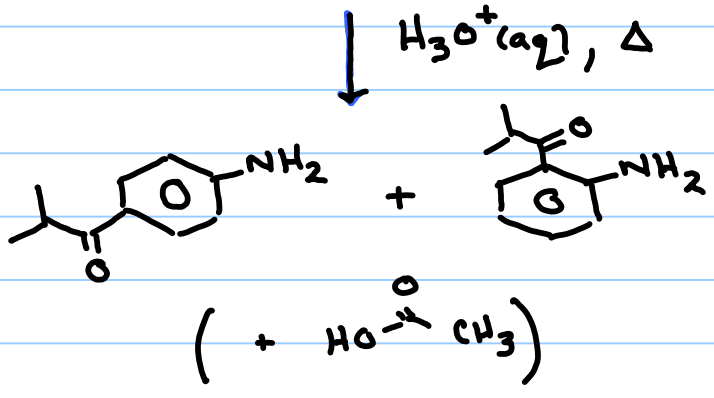
AMIDE

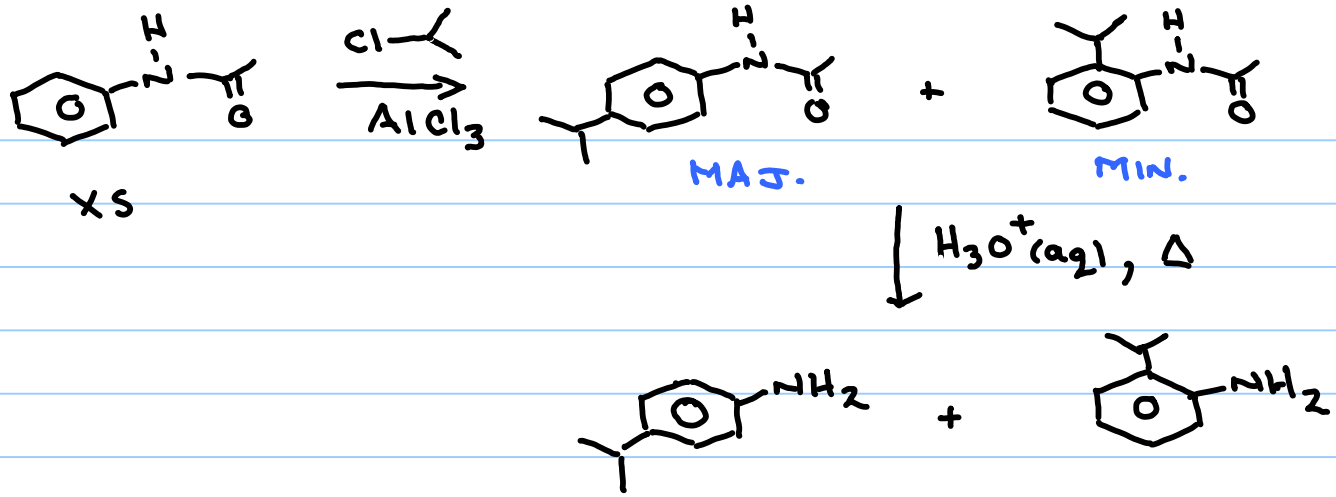
- MUCH LESS LEWIS BASIC
- STILL O-/P- DIRECTOR

NOW WONDERFUL FOR FRIEDEL-CRAFTS CHEM



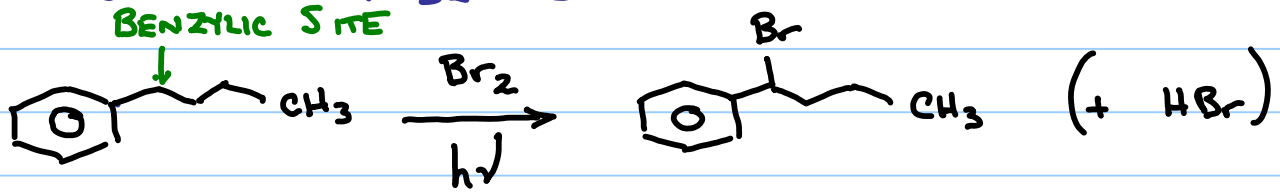
MAJ. MIN.





4. BENZYLIC HALOGENATION (BROMINATION, CHLORINATION)

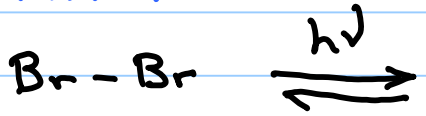
- ON ALKYLBENZENE



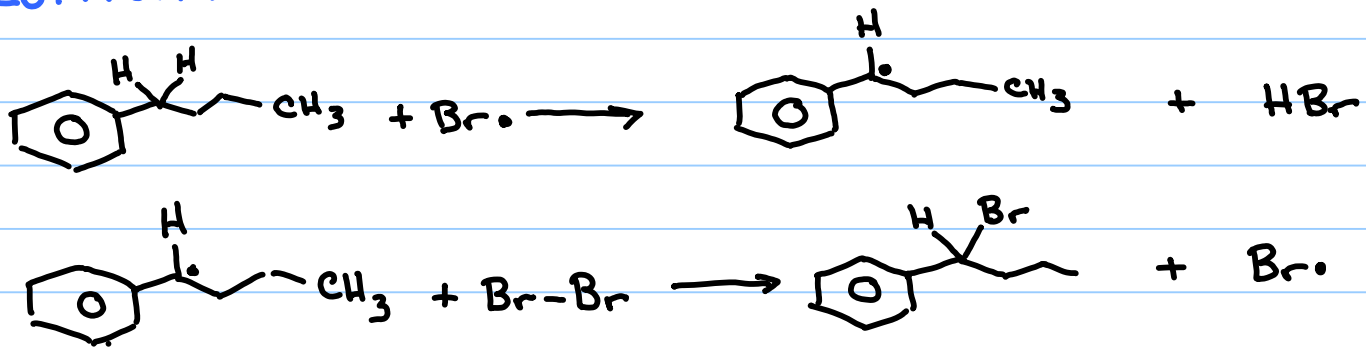
VIA A RADICAL CHAIN MECHANISM

INITIATION, PROPAGATION (2), TERMINATION STEPS

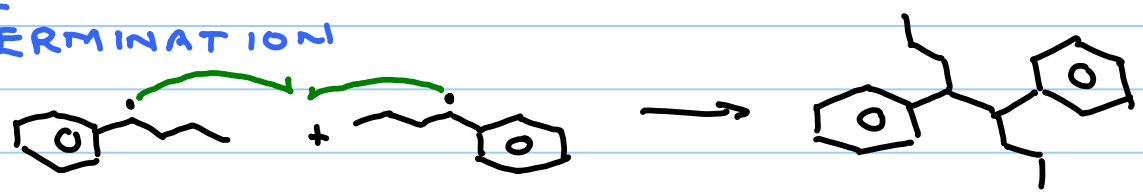
INITIATION



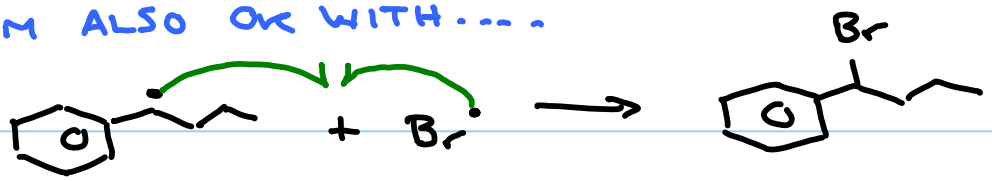
PROPAGATION



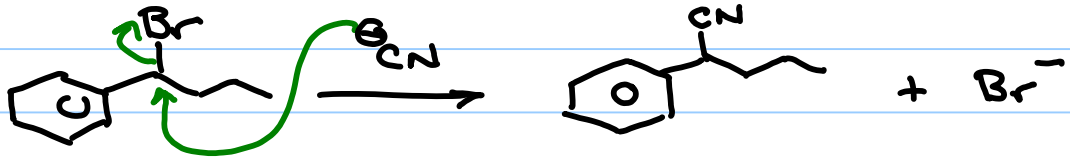
TERMINATION



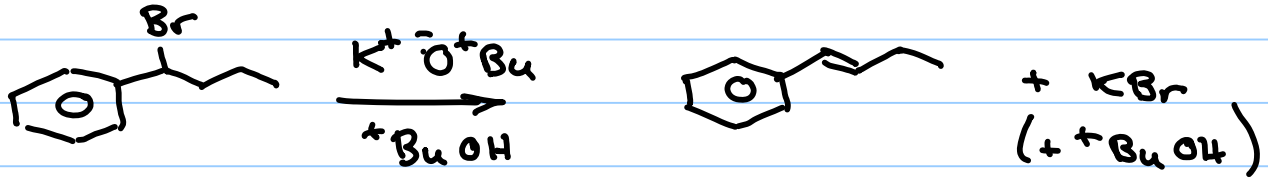
I'M ALSO OK WITH ....



BENZYLIC BROMIDES ARE GREAT FOR S_N2 RXNS

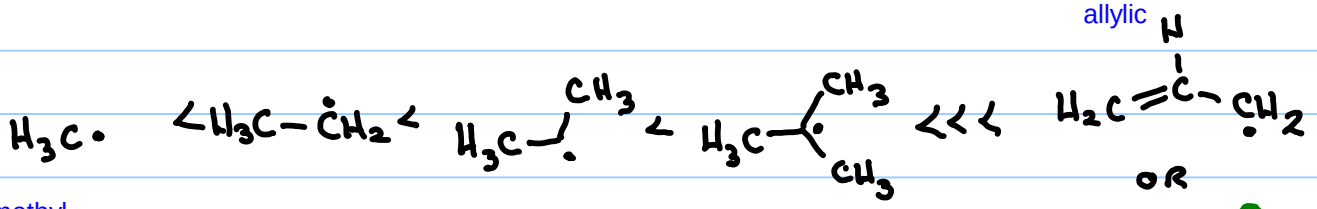


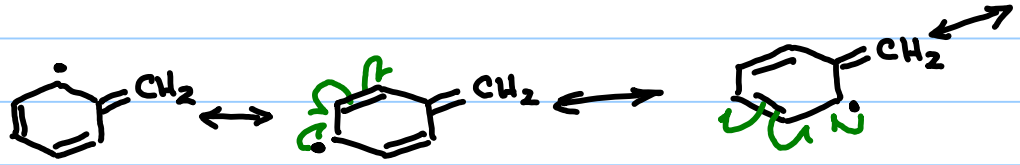
E2 ELIMINATIONS



WHY BENZYLIC SITE ?

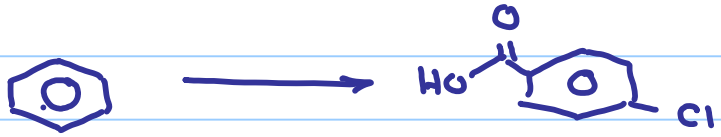
IN RADICAL STABITY



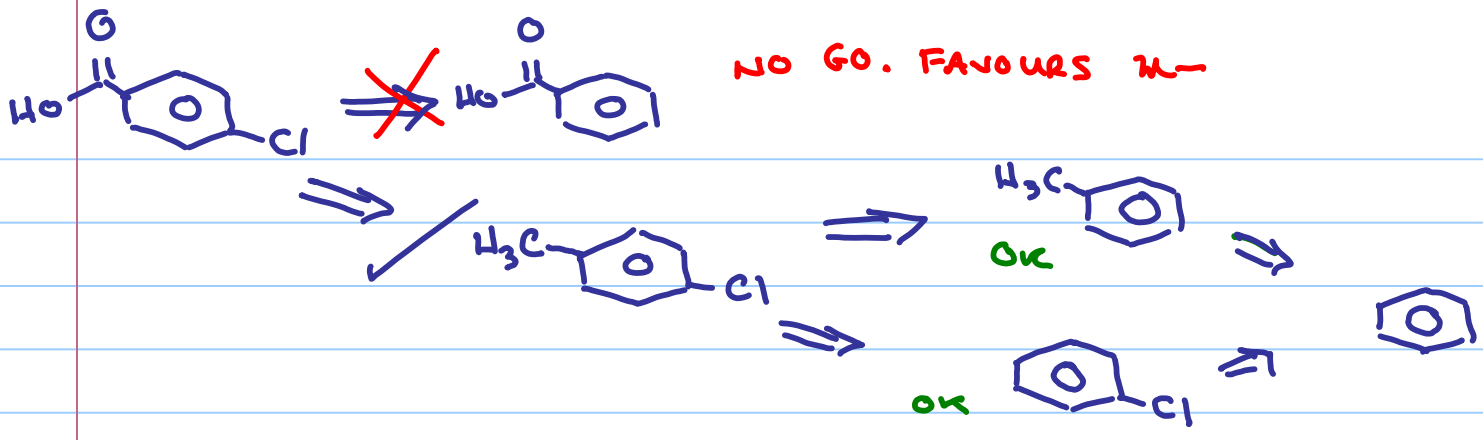


SYNTHESIS Q.

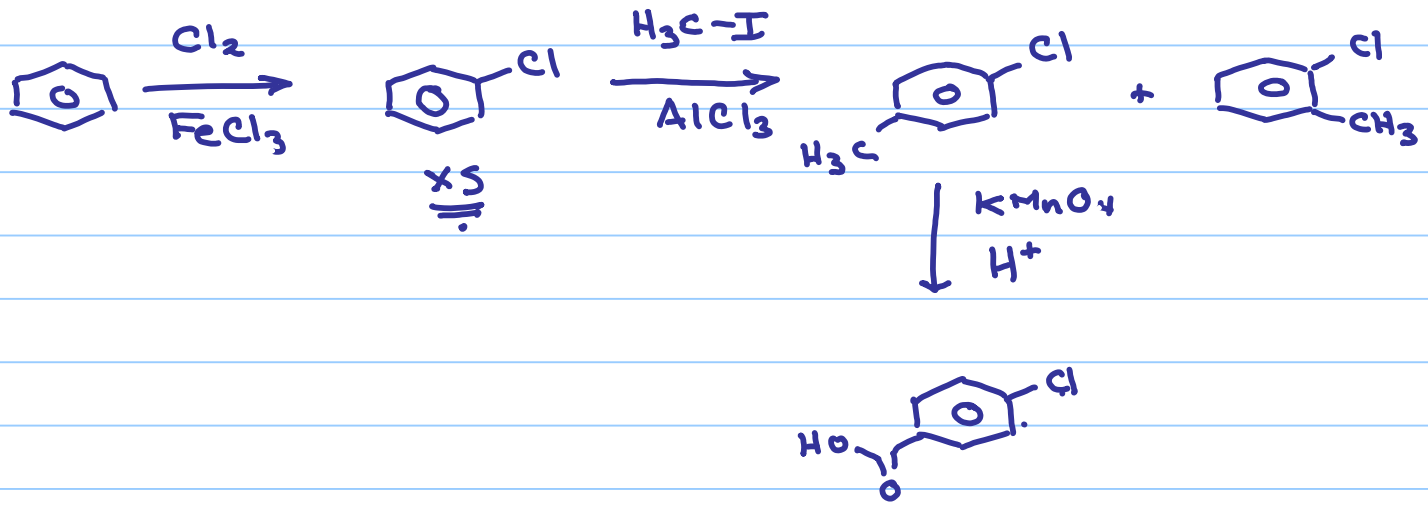
2015



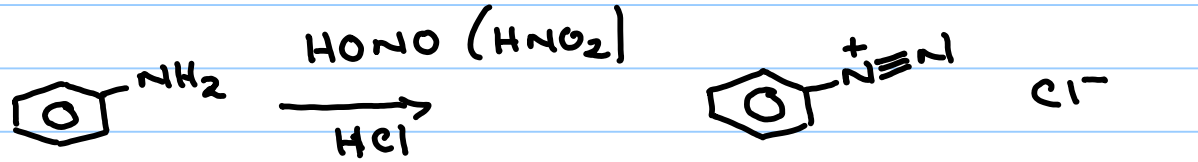
HINT: WORK BACKWARDS FROM PROD.



MY ANSWER



5. Diazonium Ions (Sandmeyer Rxn.).



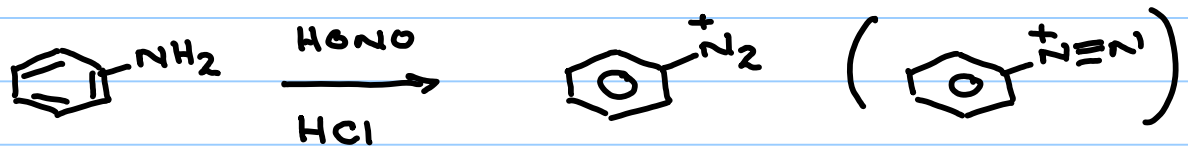
Diazonium Ion

Very reactive, but can be isolated.

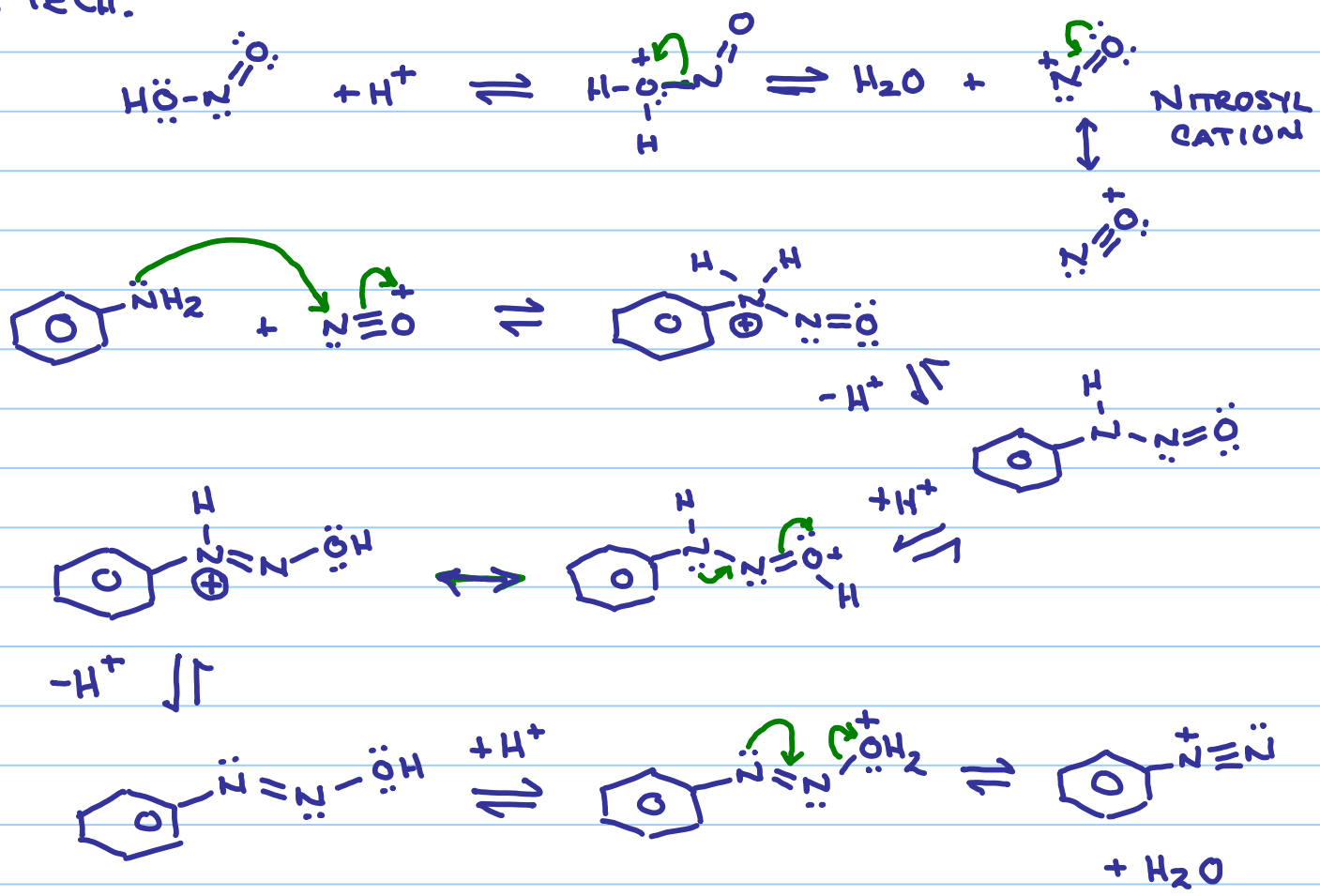
LECTURE 8

Note Title 1/31/2017

5) DIAZONIUM SALTS (SANDMEYER RXN)



MECH.

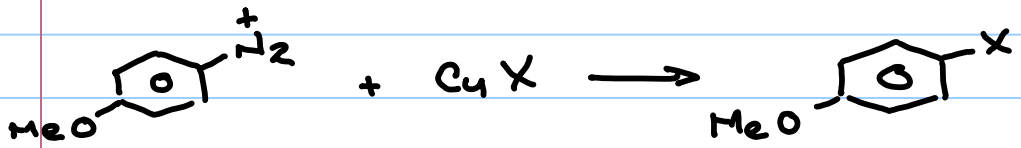


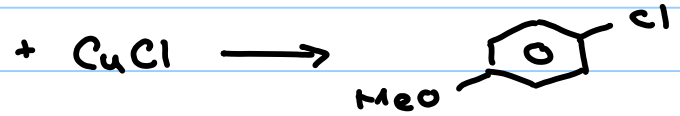
DIAZONIUM SALTS

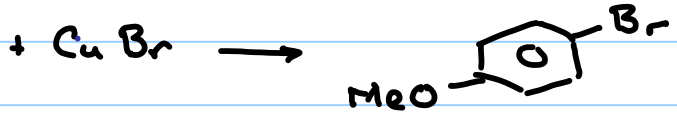
- V. REACTIVE
- NORMALLY GENERATE & REACT THEM IMMEDIATELY.

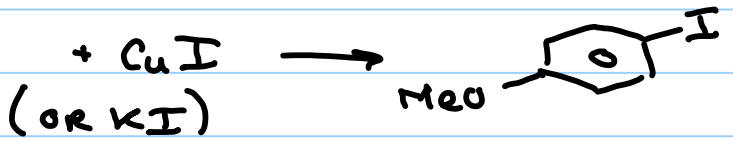
RXNS:

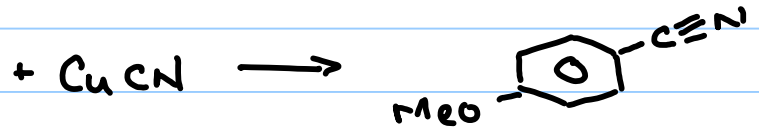
1) Rxns with Cu^{+1} Salts



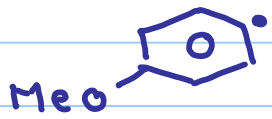






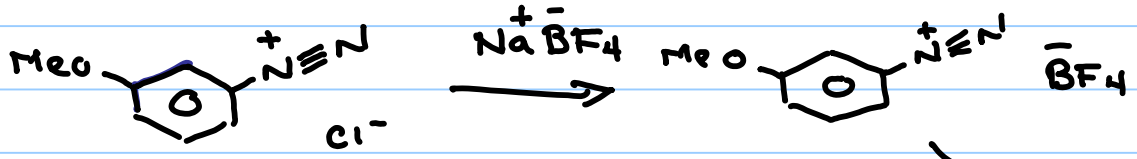


These all go through

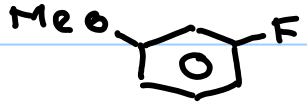


aryl radical

2) Putting in Fluoride



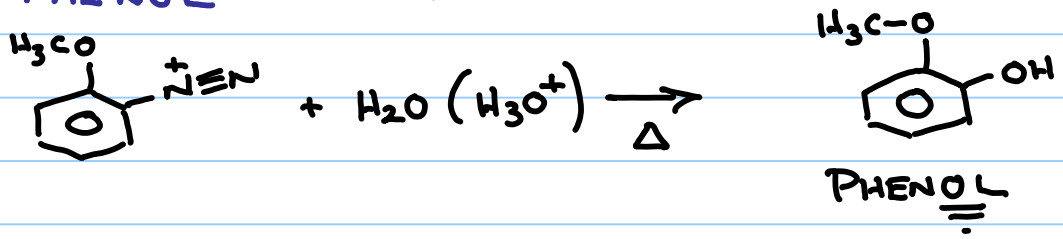
Schiemann Rxn.



Goes by an Aryl Cation

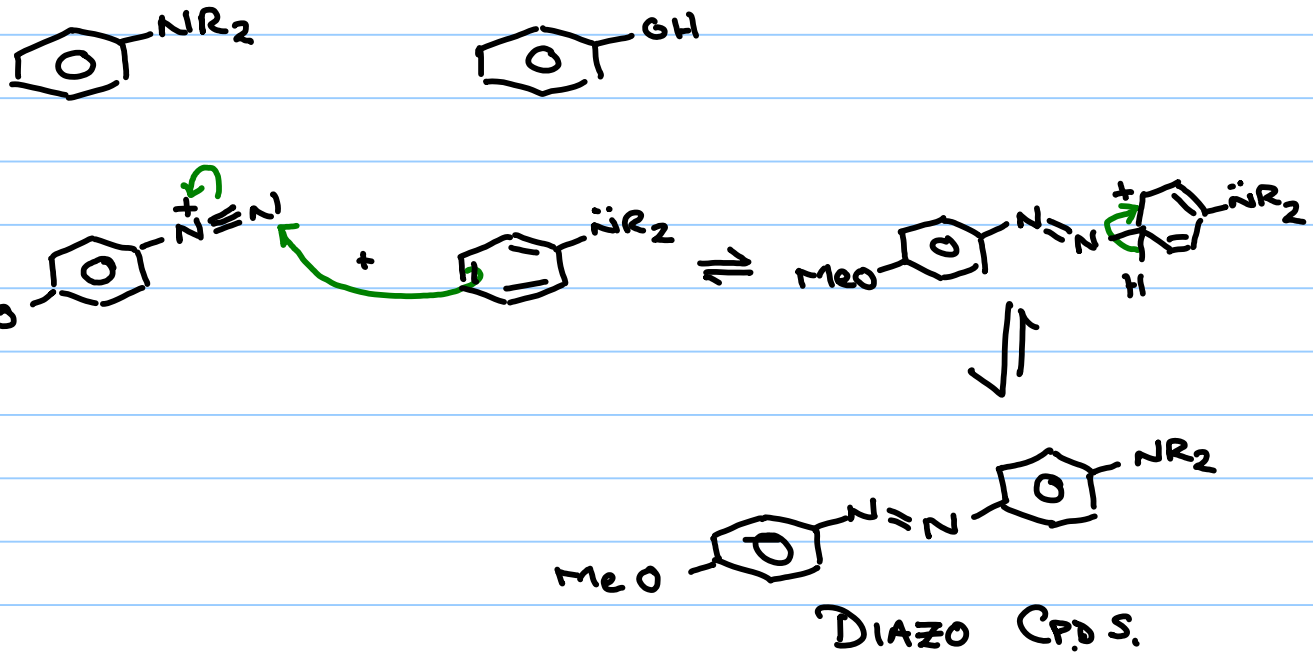
V. unstable - can only get from diazonium salts, since N_2 is fantastic leaving group

3) Phenol Synthesis



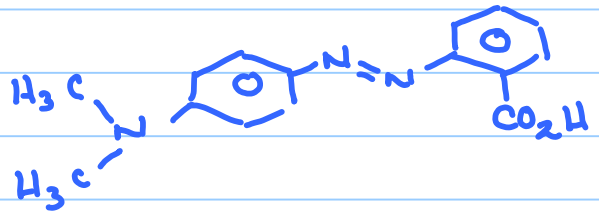
4) Diazo Compound Synthesis.

- With Really Electron Rich Benzenes



These are Highly Coloured

∴ Dyes.



Methyl Red

Red @ pH < 4.4

Yellow @ pH > 6.2

END OF TEST #1 MATERIAL

Here A - L

1120 Erie M - Z

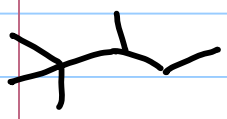
THURS: FEB. 9 60 min.

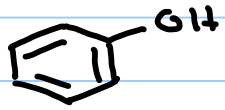
TUES FEB. 7 2ND HALF OF LECTURE IS Q + A.

PHENOLS  NOT 

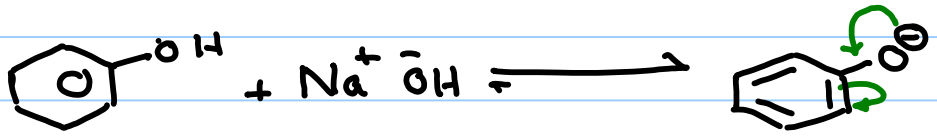
A PHENYL SUBSTITUENT

- IMPORTANT PROPERTIES
  - PHENOLS ARE A BIT ACIDIC

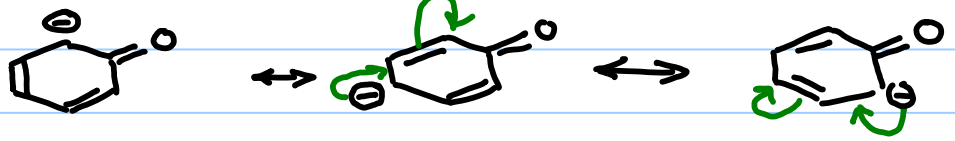
 pka ≈ 16



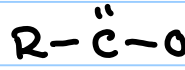
pka ≈ 10



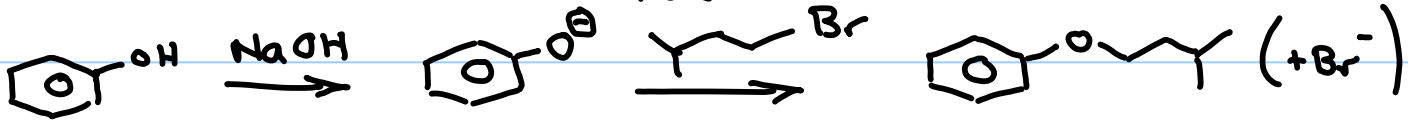
PHENOXIDE ION



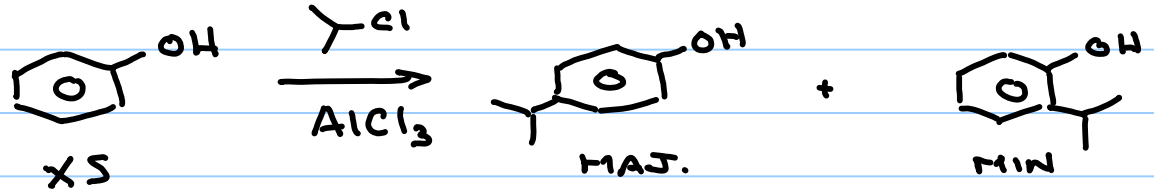
CAN THINK OF A PHENOL AS BEING "HALF WAY" TO A CARBOXYLIC ACID

 pka ≈ 4-5

SUBSTITUTION ON OXYGEN

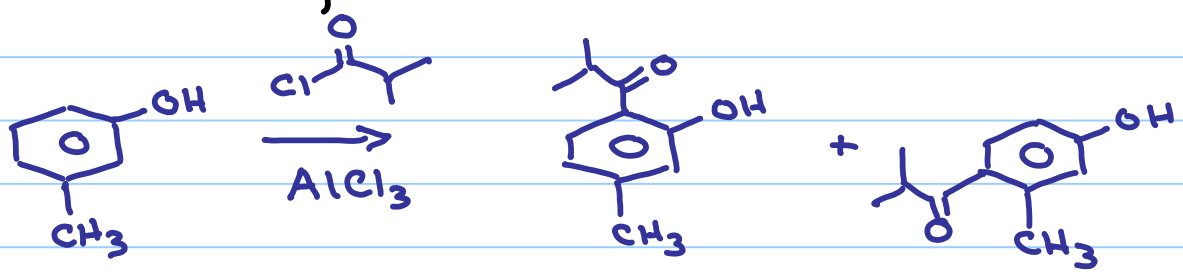


VERSUS SUBSTITUTION ON CARBON

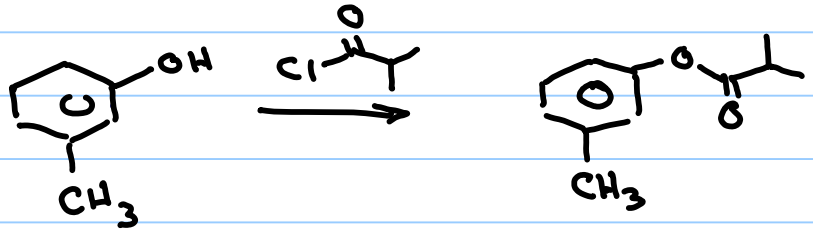


FOR ACYLATION RXNS, IT'S SIMILAR.

W LEWIS ACID, RXN GOES ON RING

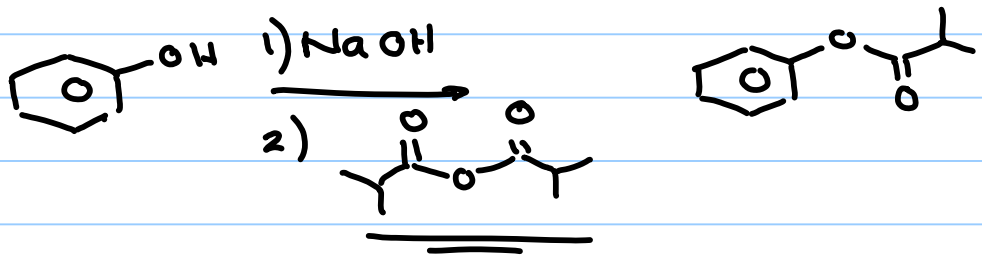


IF NO LEWIS ACID, RXN GOES ON 'O' ATOM



(NOTE: TYPICALLY A WEAK BASE I.E.  IS ADDED
SO BI-PRODUCT IS  Cl^-)

- ALTERNATIVE
  - ANHYDRIDE CAN BE USED TOO, AS LONG AS YOU ADD A BASE



Lecture 9

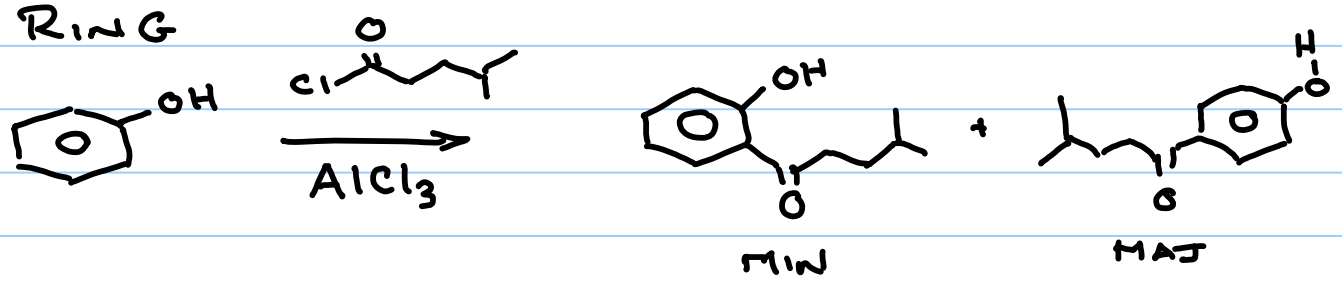
Note Title 2/2/2017

Recall Test #1 - Thurs Feb 9
10 - 11 Am
A-L Here ; M-Z 1120 Erie

Phengls.

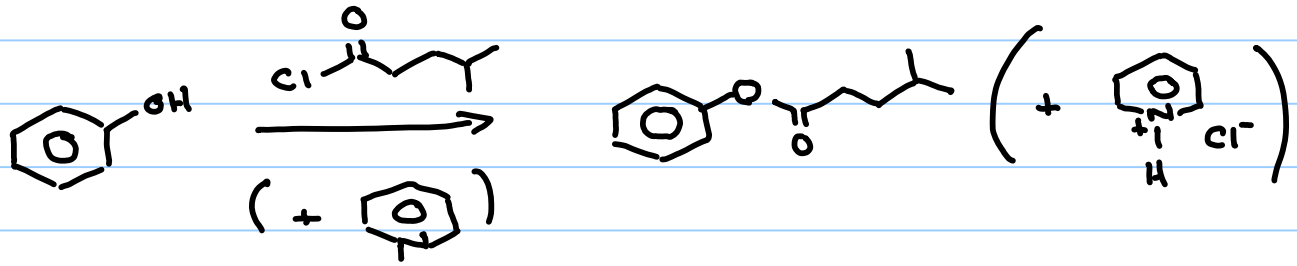
- Acylations.

- If you add a Lewis Acid, Acylation goes on ring

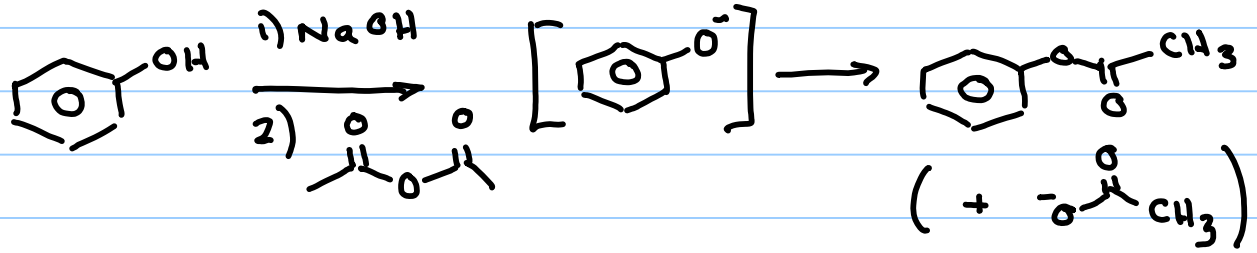


min maj

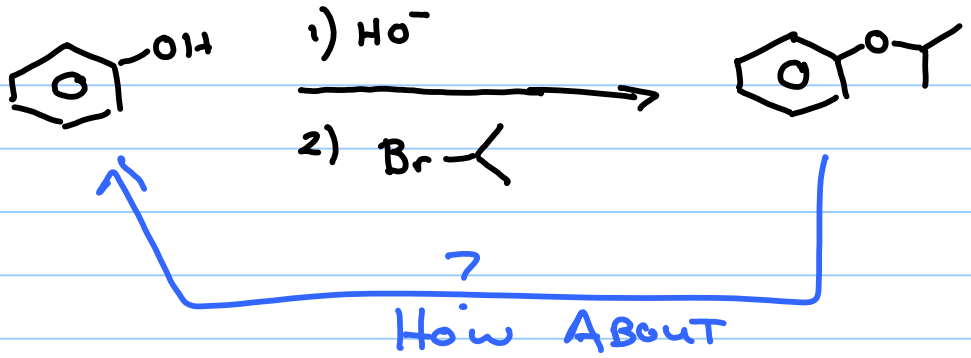
- If Lewis Acid is left out, Rxn goes on O atom



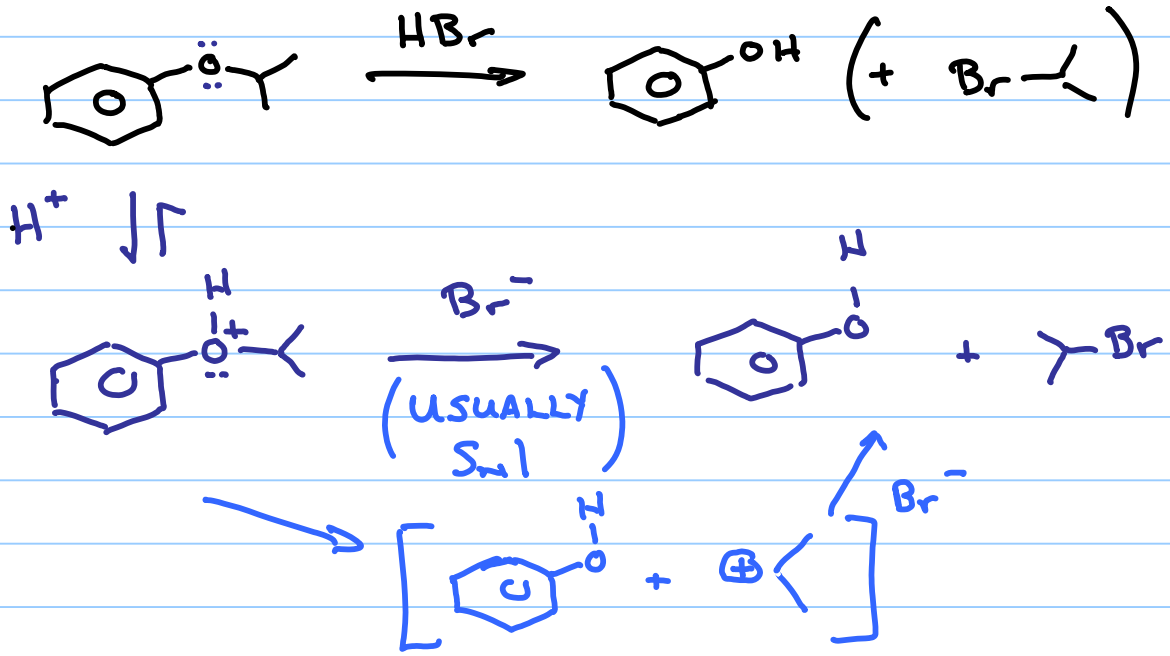
- Anhydrides will also do this, but now a Base is required



WE'VE SEEN

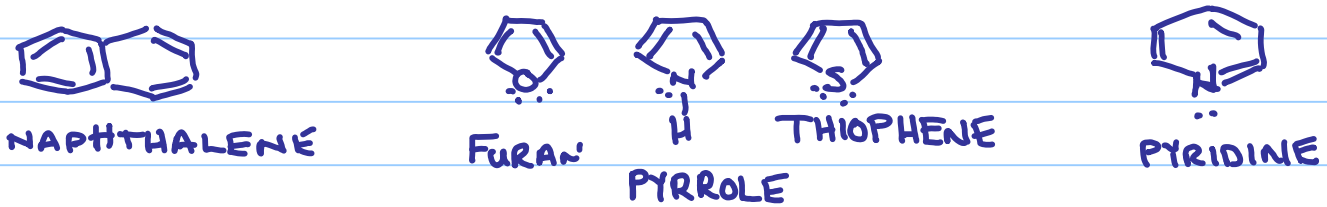


– Can be Done ...

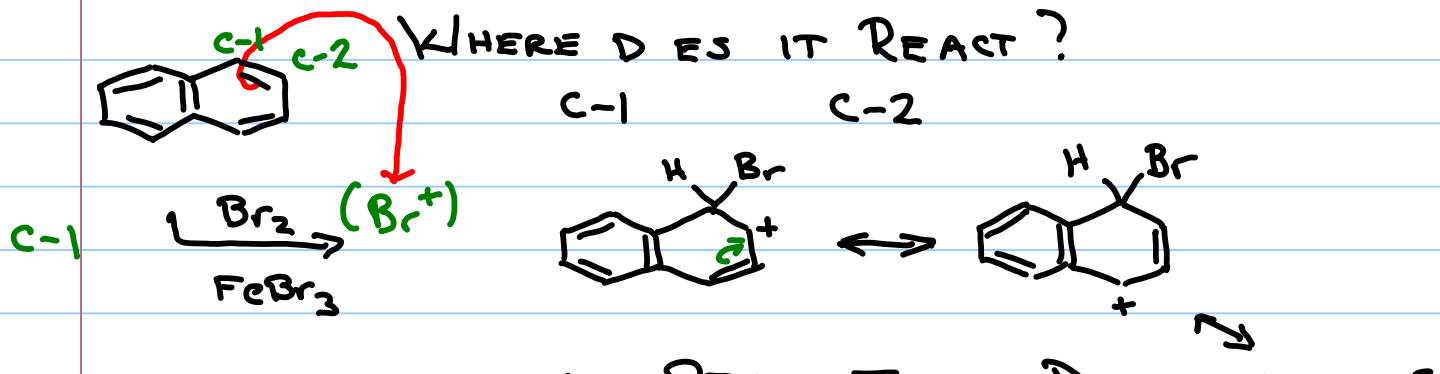


Other Aromatic Systems

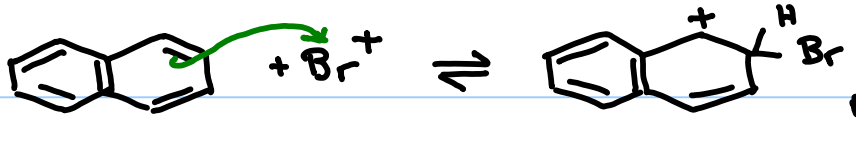
Karty 23.9



Where does it react?



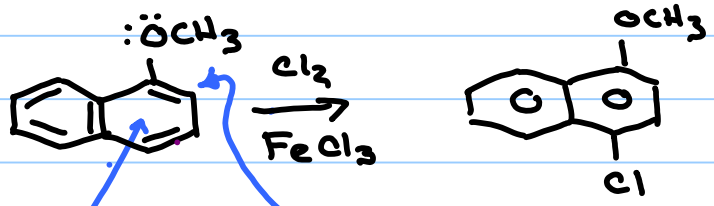
C-2



OTHER RESON. FORMS DEAROMATIZE OTHER RING

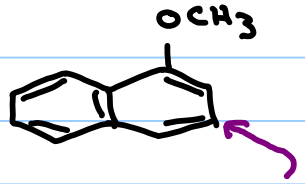
∴ RXN GOES ON C-1, SINCE 2 "BEST" RESONANCE FORMS THAT DON'T DEAROMATIZE OTHER RING

EDG C-1

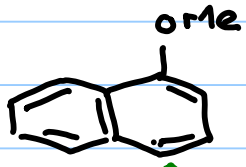


MORE e⁻ RICH RING

o- SITE ACTIVATED BY OMe ✓
C-2 TYPE ✗

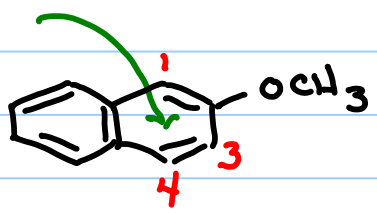


π- SITE NOT ACTIVATED BY OMe ✗
C-2 TYPE ✗



p- SITE ACTIVATED BY OMe ✓
C-1 TYPE ✓
∴ WINNER

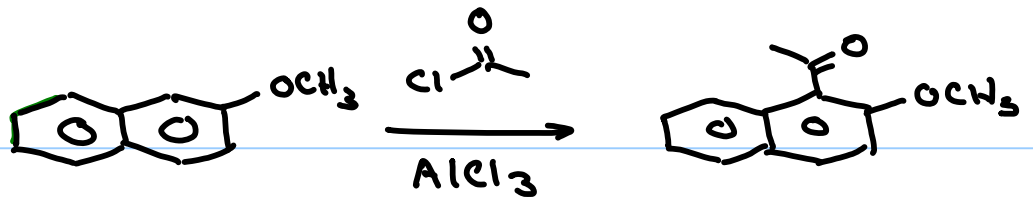
MORE e⁻ RICH RING



SITE C-1
o- WRT OCH_3 ACTIVATED ✓
C-1 TYPE POSITION ✓

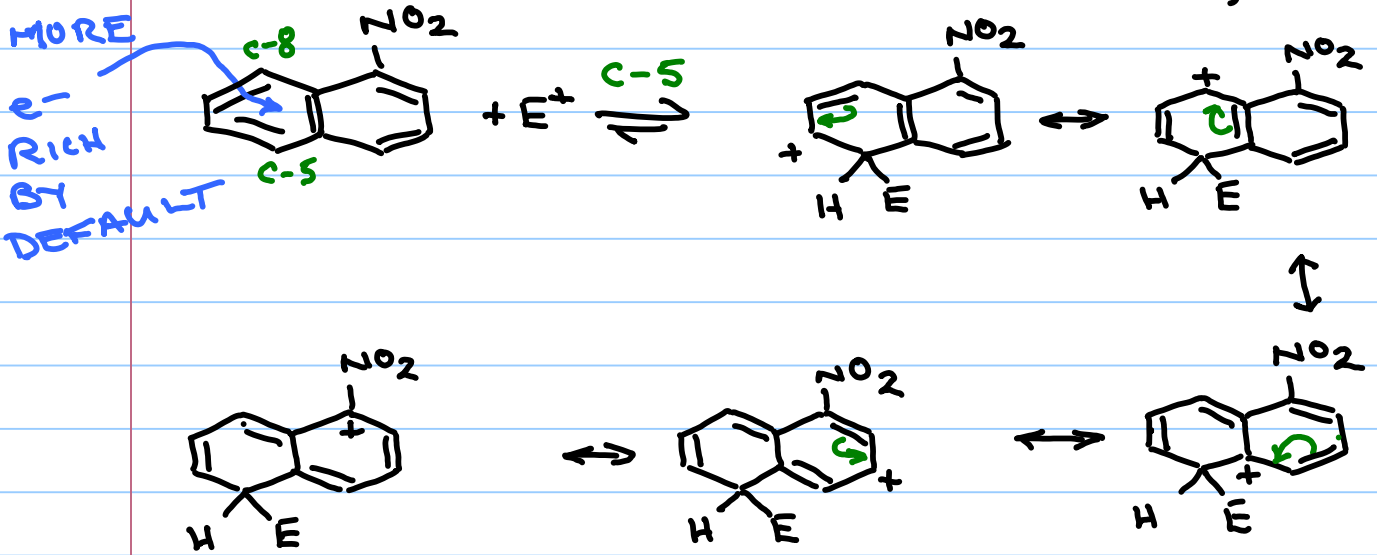
C-3
o- ACTIVATED BY OCH_3 ✓
C-2 TYPE ✗

C-4
π- NOT ACTIVATED BY OMe ✗
C-1 TYPE ✓

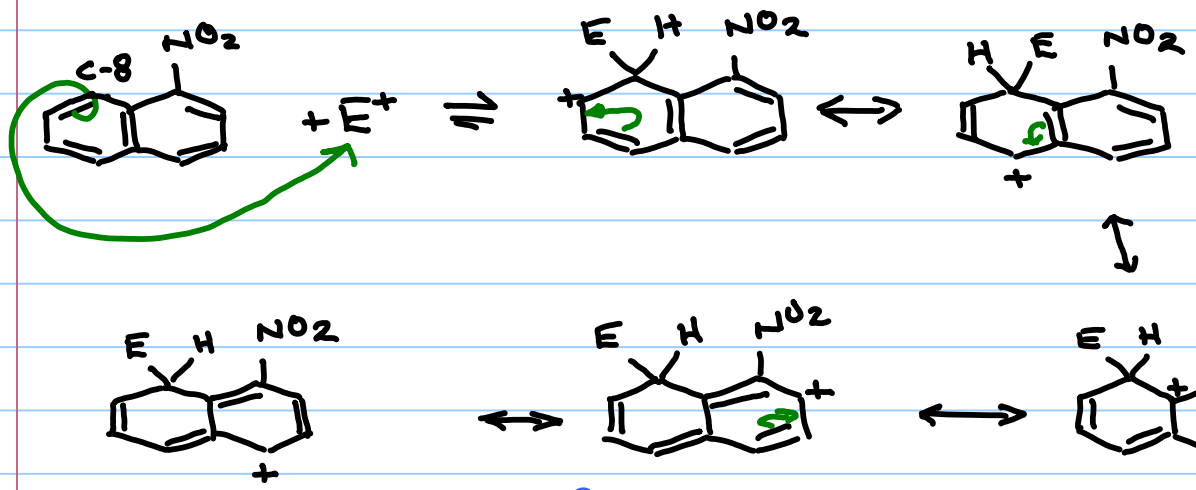


C-1 !

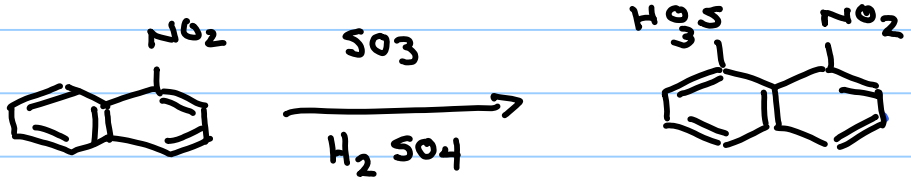
HOW ABOUT EWG (m- DIRECTING, DEACTIVATING)



BAD - DISFAVOURED



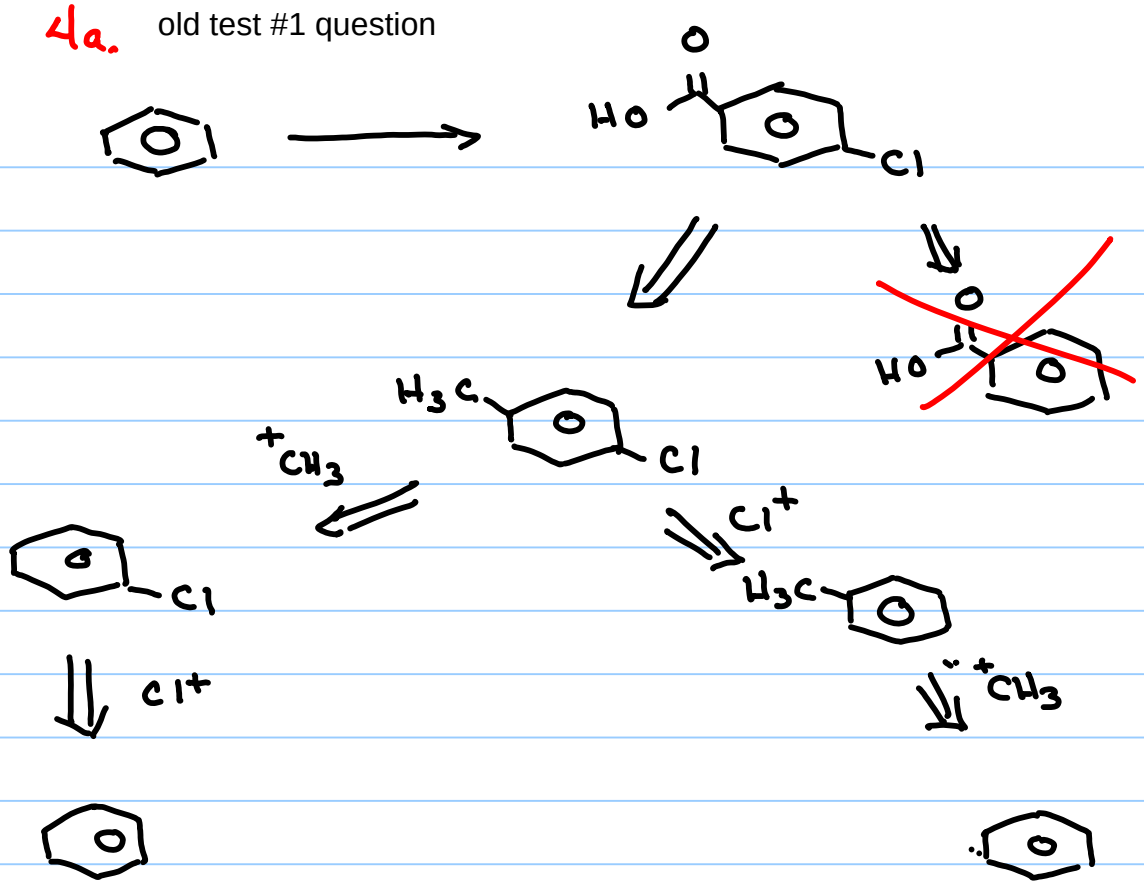
NEVER PUT "+" CHARGE ON C WITH THE EWG - RELATIVELY GOOD



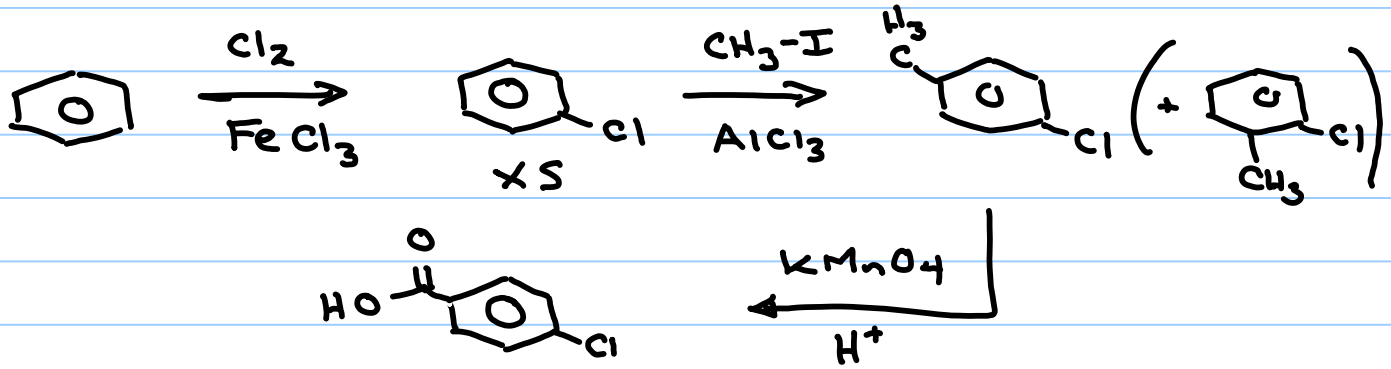
C-8 !

TRY

2015 4a. old test #1 question



SOLN:



Note: an answer where you 'methylate' first, then chlorinate, then finally do the KMnO4 oxidation would be just as acceptable.

LECTURE #10

Note Title 2/7/2017

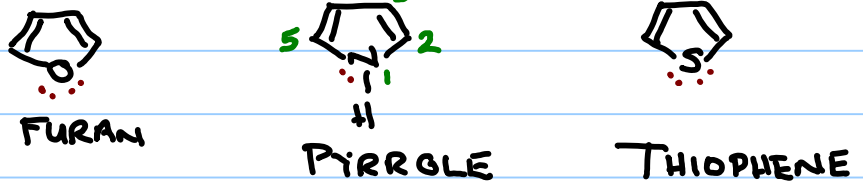
RECALL - TEST #1 THURS FEB 9 10-11 AM

A-L HERE

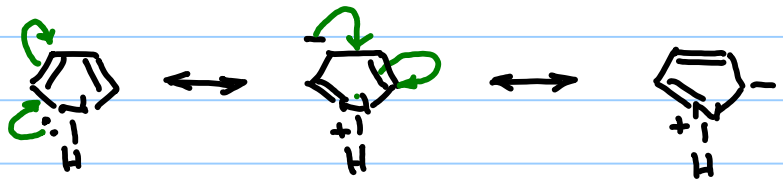
M-Z 1120 ERIE

HETEROCYCLES

GROUP 1



LONE PAIR AFFECTS REACTIVITY



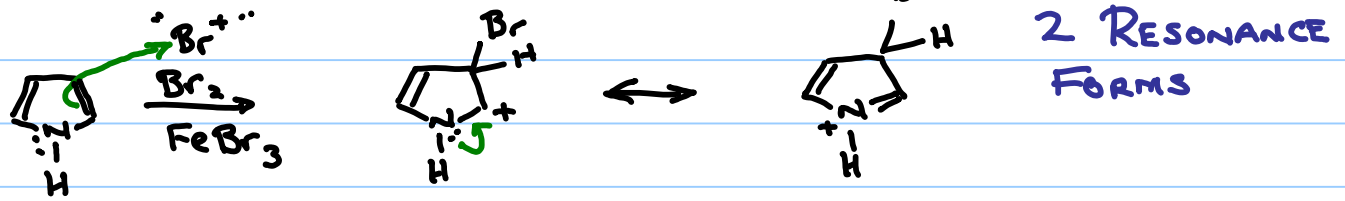
∴ C ATOMS ARE e⁻ RICH

∴ REACT FASTER THAN BENZENE

"π - EXCESSINE HETEROCYCLES"

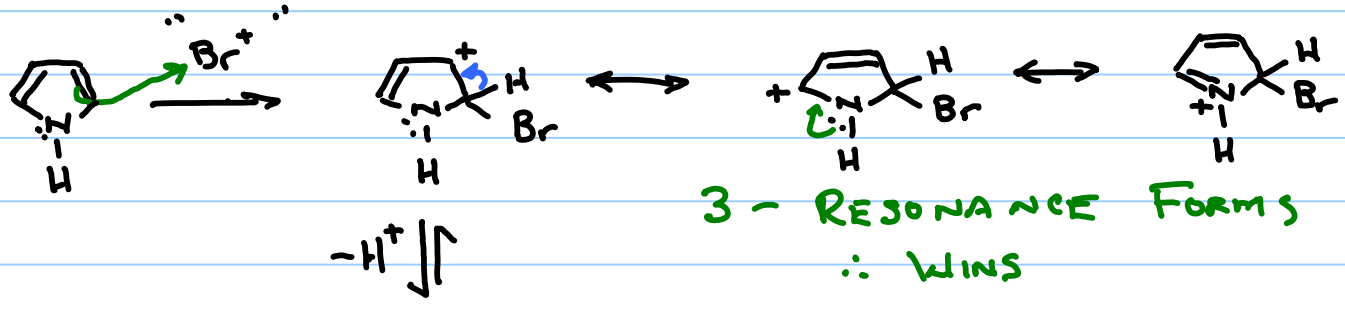
SO WHERE DO THEY REACT ?

C-3



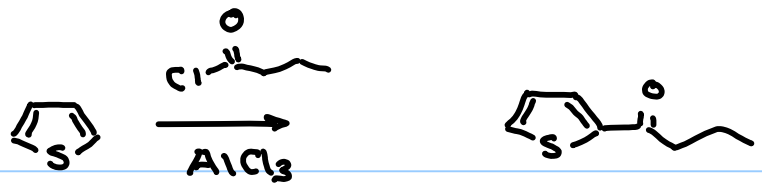
2 RESONANCE FORMS

C-2

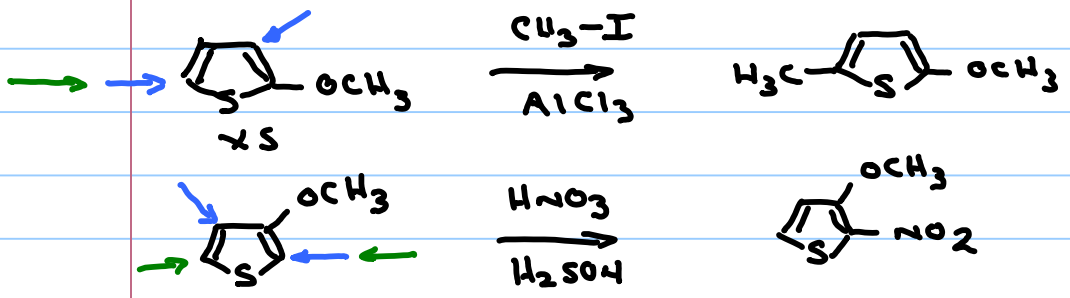


3 - RESONANCE FORMS

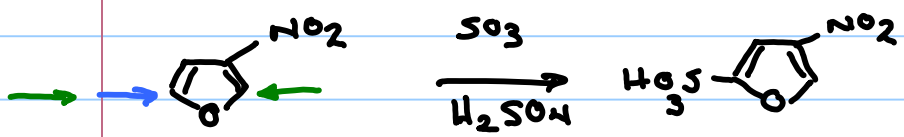
∴ WINS

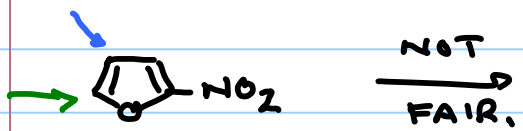


ω EDG's ? Electron Donating Groups ?

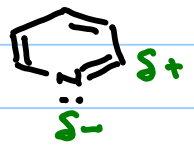


ω EWG's Electron With Drawing Groups





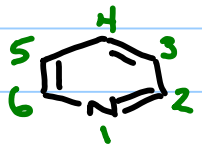
- Pyridine



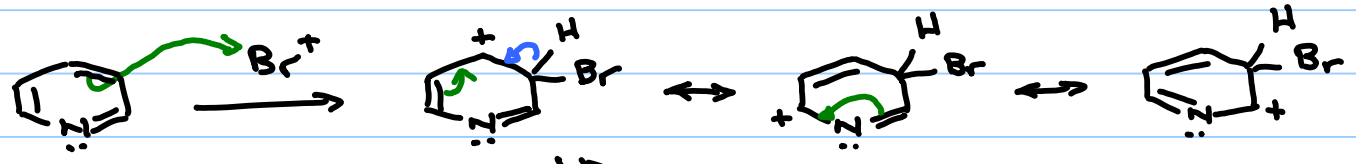
∴ Carbon Atoms are e⁻ Deficient

∴ Less Reactive than Benzene

"π- Deficient Heterocycle"



C-3 Rxn



Avoids Putting + Charge on 6 Valence e⁻ N

Relatively Good

C-3 Preferred when Rxn Occurs

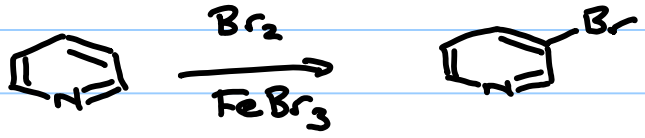
Lecture 11

Note Title 2/14/2017

Recall

Pyridine

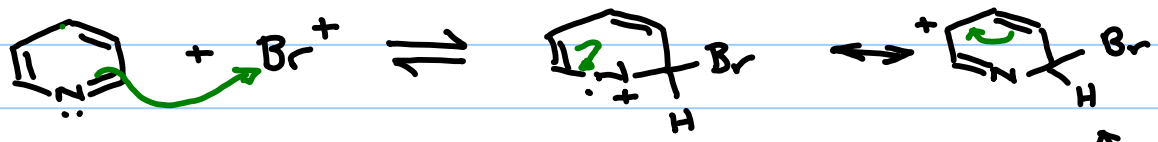
Somewhat e^- Poor



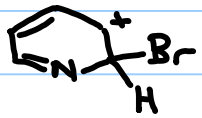
C-3 Rxn is ok

What About C-2, C-4 Rxn Possibilities ?

C-2.

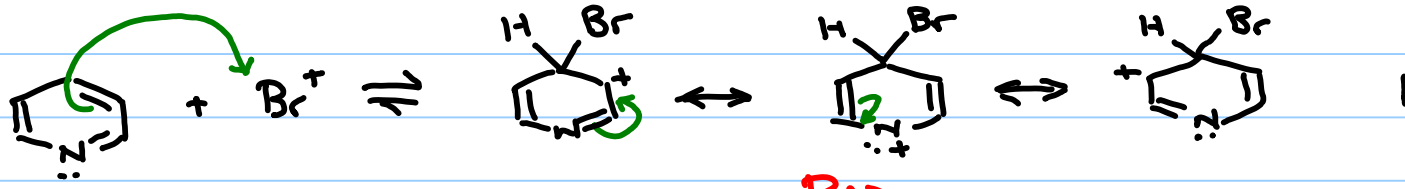


Bad - 6 valence e^- N^+



Won't Go

C-4



Bad 6 Valence e^- N^+

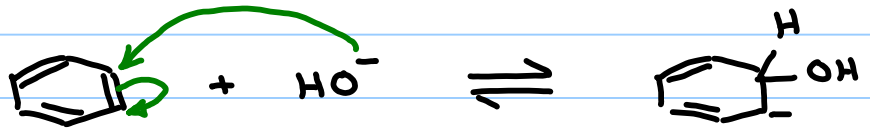
∴ Won't Go

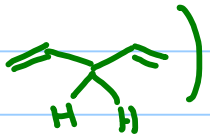
∴ When Rxn Goes on Pyridine, it is Slowed, and Rxn Goes at C-3 By Default.

Nucleophilic Aromatic Substitution

- Since Benzenes have an electron rich π-System this is not as common as Electrophilic Subst., But it <u>Can</u> Go

LET'S CONSIDER ITS BASICS



pka ≈ 15.7 pka ≈ 35 (USING  AS A GUIDE)

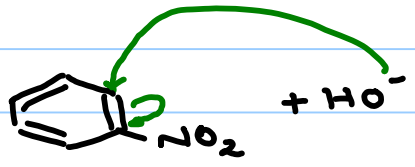
- ALSO WORKING AGAINST 120-150 KJ/mol OF AROMATIC STABILIZATION

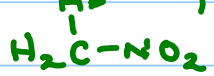
PROBLEM #1 ∴ K_{eqn} <<<<<<< 1 unuseably small

PROBLEM #2 H^+ CAME OFF IN ELECTROPHILIC SUBST.
- EASILY ACCESSIBLE
BUT HERE $H^\ominus$ WOULD HAVE TO LEAVE
- THIS IS A TERRIBLE, TERRIBLE LEAVING GROUP

THESE ISSUES CAN BE SOLVED

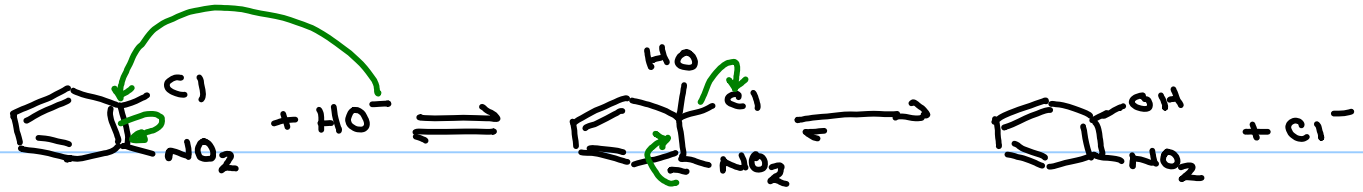
#1 LET'S CONSIDER A STRONG EWG; I.E., NO_2

NOW 

pka ≈ 15.7 pka < 10 USING. 

∴ K_{eqn} IS NOW REASONABLE AND ACCESSIBLE

#2 LET'S CONSIDER A GOOD LEAVING GROUP, I.E., Cl, ON THE RING



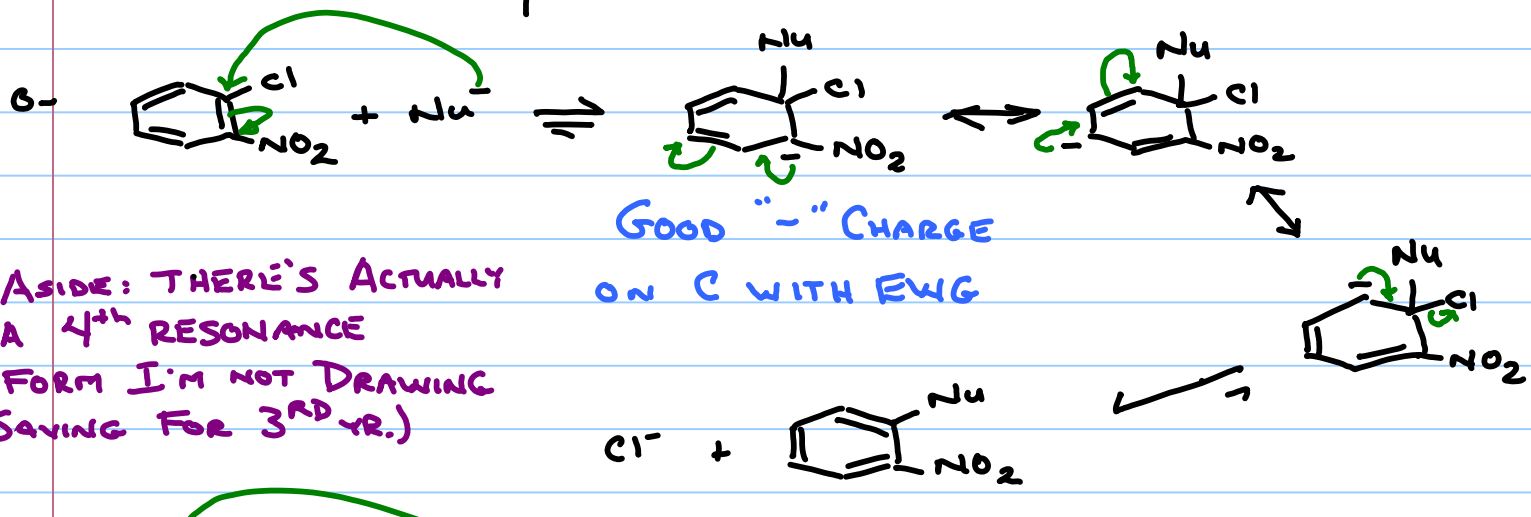
- NOW WE ARE IN BUSINESS - THIS WILL WORK

SO THE REQUIREMENTS FOR NUCLEOPHILIC AROMATIC SUBSTITUTION ARE:

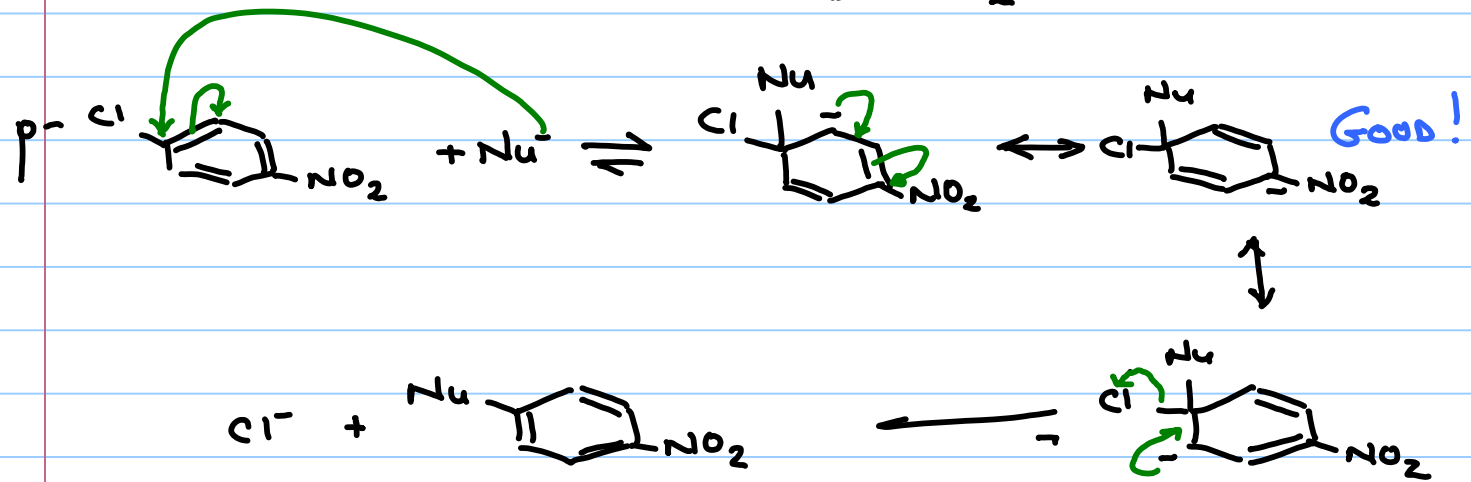
1) A LEAVING GROUP.

2) A GOOD EWG EITHER ORTHO- OR PARA- TO THAT LEAVING GROUP

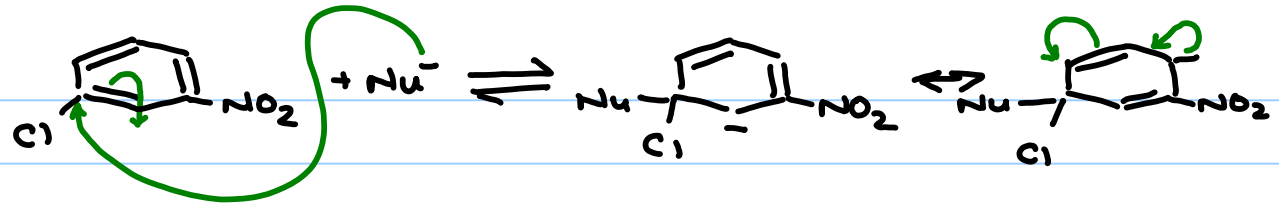
- WHY ONLY O- / P- ?



ASIDE: THERE'S ACTUALLY A 4TH RESONANCE FORM I'M NOT DRAWING (SAVING FOR 3RD YR.)



But ...



Not Nearly as Good

"−" Charge Never on C Atom with EWG

∴ Won't Go.

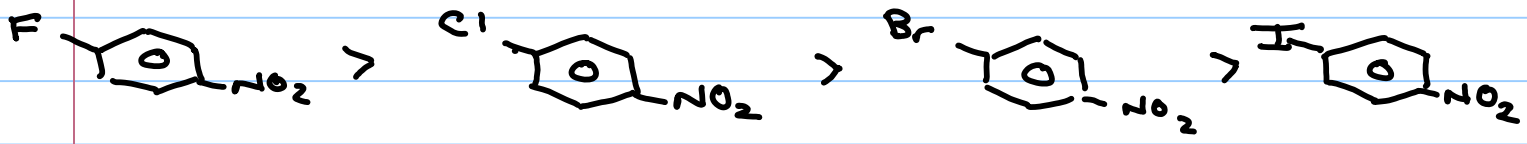
Individual Features

a) Leaving Groups – Superficially Backwards (!)

- Recall in S_N1 & S_N2 Reactions, For Leaving Groups

$$I^{\ominus} > Cl^{\ominus} > Br^{\ominus} \gg F^{\ominus}$$

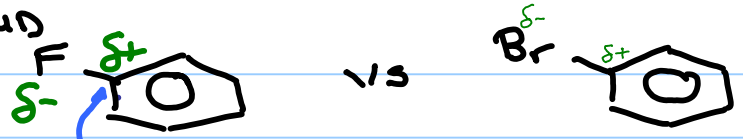
- But in Nucleophilic Aromatic Substitution



- Reason – This is a Two Step Mechanism, with The 1st one as Rate Determining (i.e. Slow)

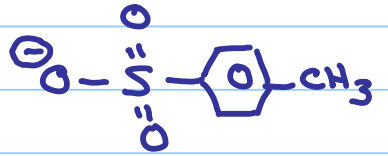
unlike SN1 or SN2, halide ion is not forming in the rds
-so relative leaving group ability is not central to rate - but electronegatvity is

AND



MORE δ+ CHARACTER DUE TO F'S EN BEING HIGH
∴ 1ST STEP FASTER

WE'LL ADD ONE MORE LEAVING GROUP.



TOLUENESULFONATE ION
(TOSYLATE)

≡ $^{\ominus}OTs$

EXCELLENT LEAVING GROUP ABOUT ≈ $I^{\ominus}$ IN S_N1/S_N2
OFTEN CALLED A PSEUDOHALIDE

IN NUCLEOPHILIC AROMATIC SUBSTITUTIONS, YOU GET

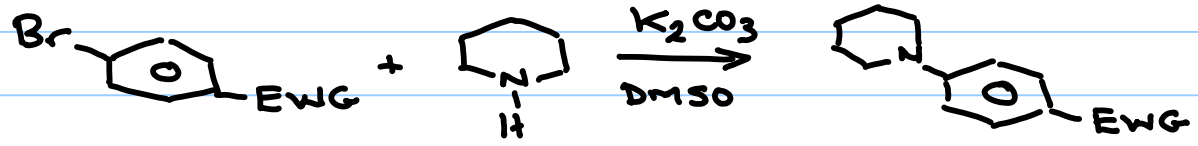
$$F^{\ominus} > TsO^{\ominus} > Cl^{\ominus} > Br^{\ominus} > I^{\ominus}$$

b) EFFECT OF ELECTRON WITHDRAWING GROUP (EWG)

NO_2 IS PRETTY MUCH THE STRONGEST EWG WE HAVE

- SOME OTHERS CAN BE USED

- SOME ACTUAL KNOWN RELATIVE RATES



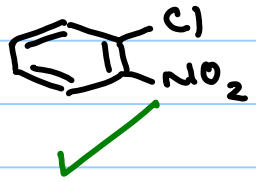
RELATIVE RATE				
$-NO_2$	$-S(=O)(=O)-CH_3$	$-C\equiv N$	$-C(=O)CH_3$	$-CF_3$
100	5.3	3.1	1.3	< 1

- So taking these two features together, here are my 'official 235 rules' for what works reasonably

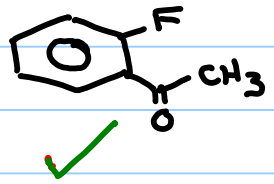
- If EWG = $-NO_2$
  - Rxn works for all halides / pseudohalides that are o- or p-

- For other EWG's (as long as they're medium strength or more)
  - Rxn works for F- only (o- and/or p-)
  - And with other halides / pseudohalides, you need two of these EWG's (o- and/or p-)

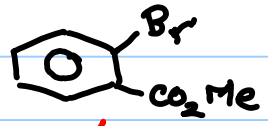
So....



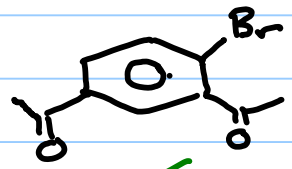
✓



✓



✗ too slow

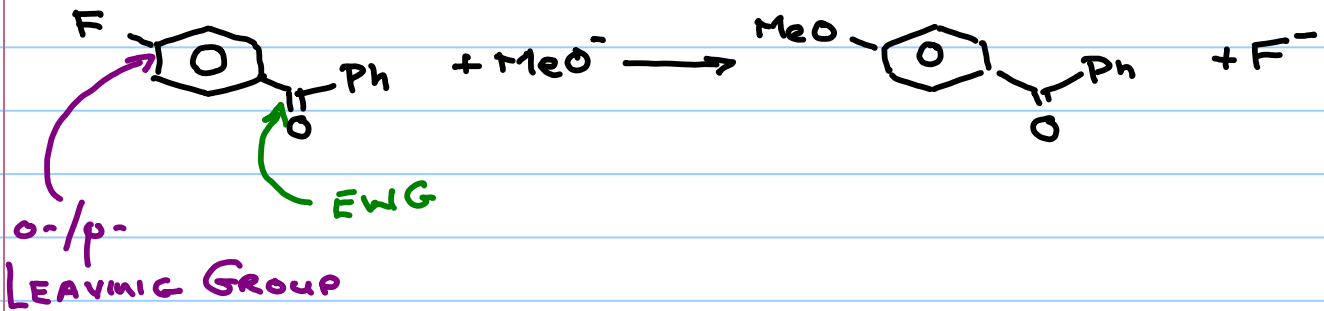


✓ one o-, one p-

LECTURE 12

Note Title 2/16/2017

NUCLEOPHILIC AROMATIC SUBST.



NUCLEOPHILE - WHAT KIND OF NUCLEOPHILES CAN WORK?

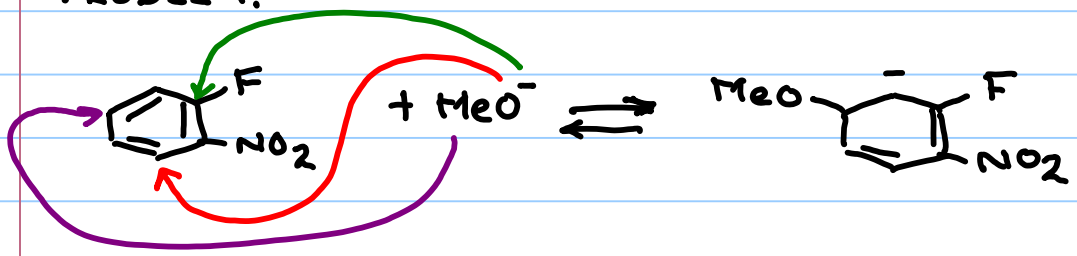
- USUALLY HETEROATOM BASED.

$RO^{\ominus}$, $HO^{\ominus}$, $^{\ominus}NH_2$, $R\ddot{N}H_2$ (NEUTRAL), RS^-, $X^{\ominus}$ (HALIDE)

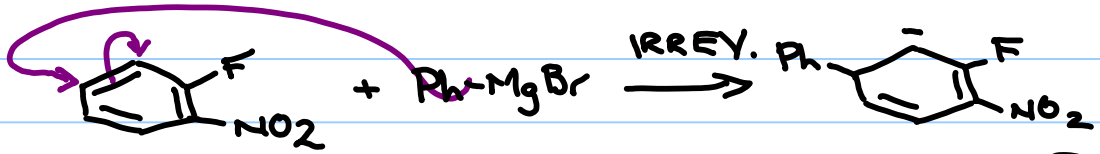
$^-N_3$ (AZIDE $^{\ominus}N=\overset{+}{N}=N^{\ominus}$)

- NOT THE SIMPLEST C NUCLEOPHILES

PROBLEM.

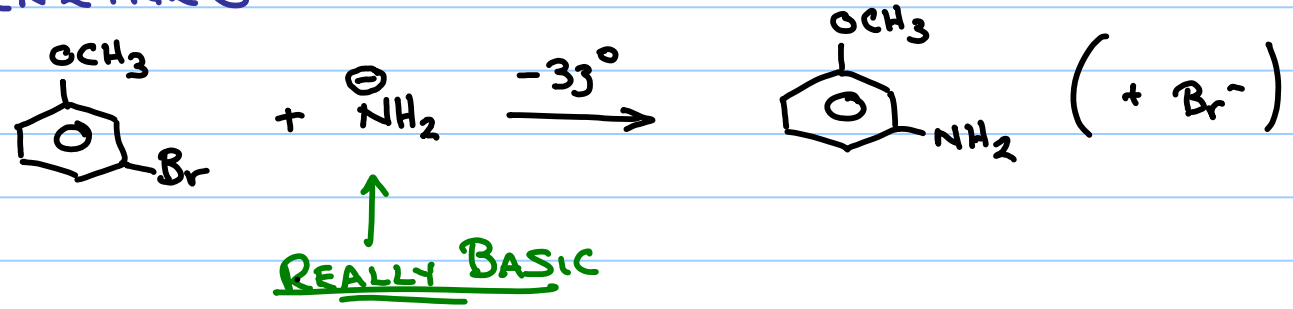


REVERSIBLE SO IT CAN COME OFF & GO AT PROPER SITE

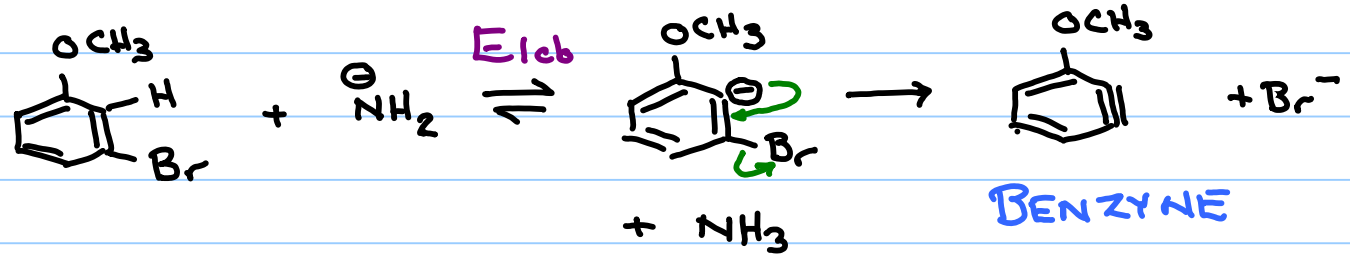


∴ GET V. BAD MIXTURES OF PRODUCTS.

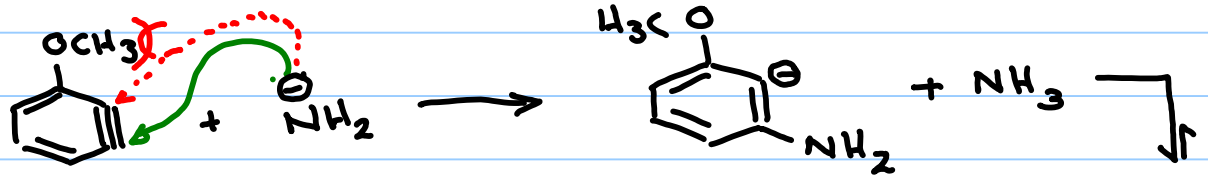
BENZYNES

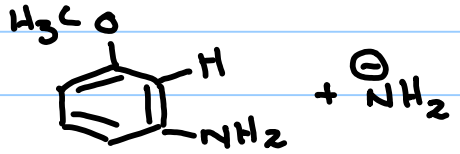


pK_a H_2O = 15.7 pK_a NH_3 = 35

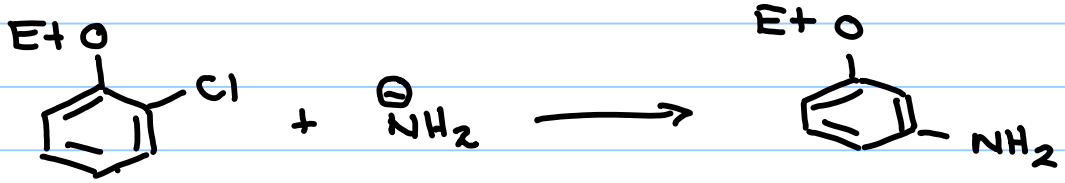


BENZYNE - V.V.V. HIGHLY ANGLE STRAINED ALKYNE
- EXISTENCE < 1 SECOND.

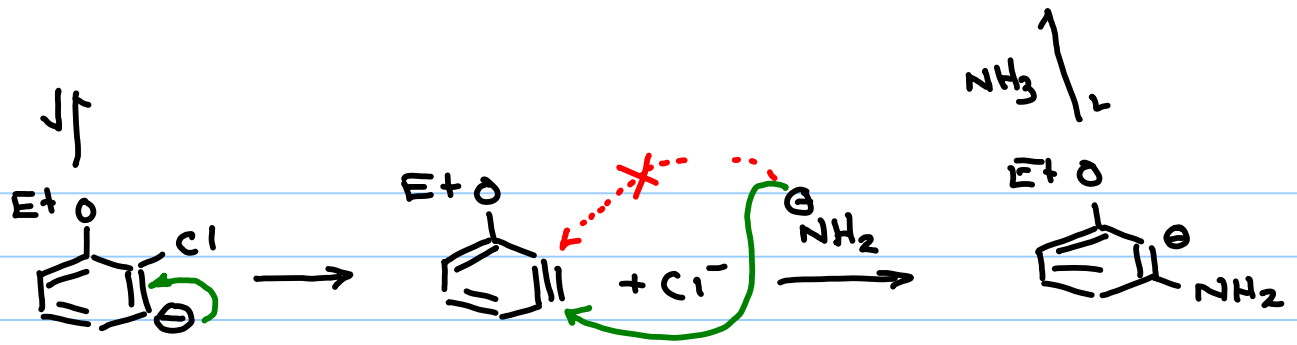


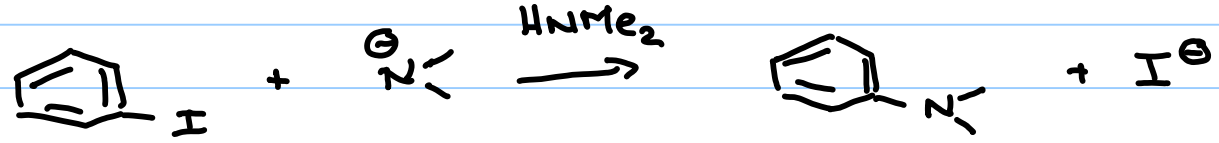


- ALTERNATE SITE OF Nu^- ATTACK SLOWED DOWN BY SUBSTITUENT - JUST ENOUGH TO DISFAVOUR IT.



- THIS FEATURE (Nu^- GOING IN AT SITE OTHER THAN WHERE LEAVING GROUP WAS) IS A BENZYNE MECHANISM GIVE-AWAY





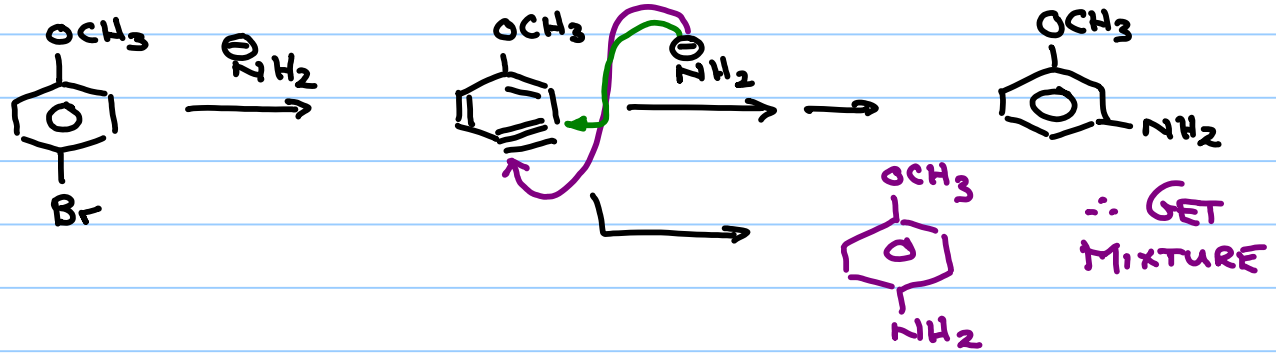
- LEAVING GROUPS.

$I^{\ominus}$, $Br^{\ominus}$, $Cl^{\ominus}$, $TsO^{\ominus}$

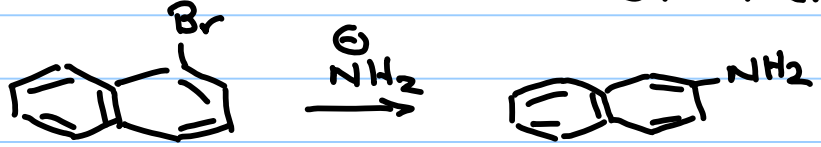
- NUCLEOPHILES.

$^{\ominus}NH_2$, $^{\ominus}NHR$, $^{\ominus}NR_2$ MOST COMMON

$HO^{\ominus}$, $RO^{\ominus}$ AT 300°C



UGLY, BUT PROPER RESONANCE FORM OF BENZYNE.

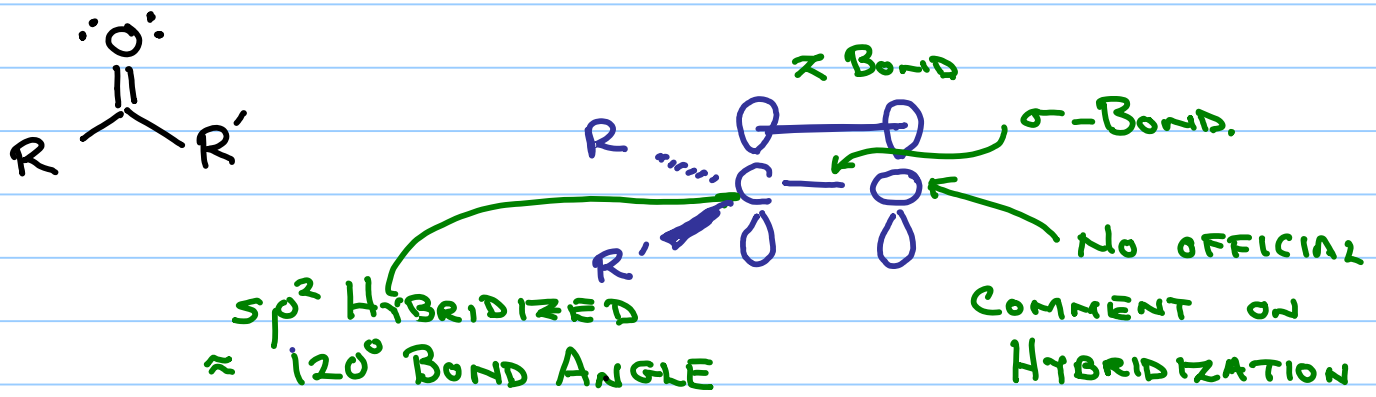


Lecture 13

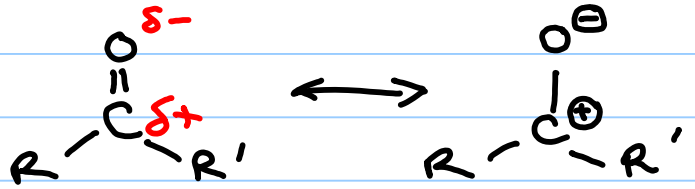
Note Title 2/28/2017

Chemistry of Carbonyl Compounds.

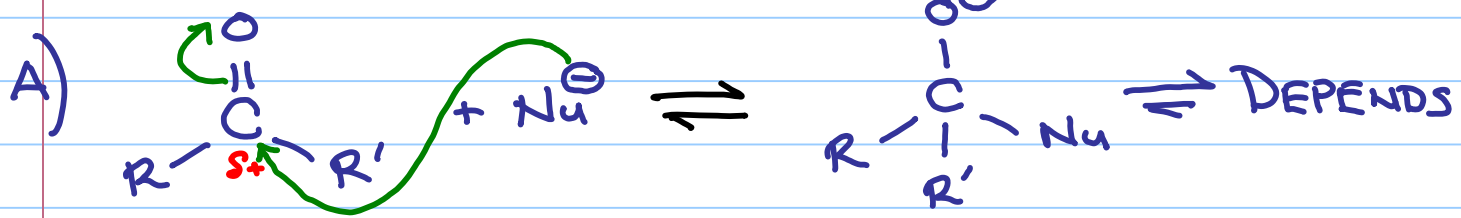
Ch 17 & 18 Karty.

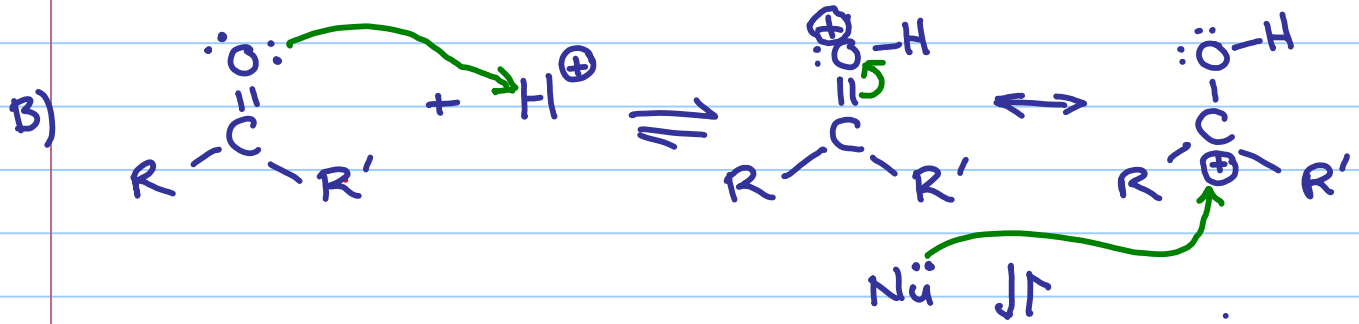


Critical - Oxygen is more En than Carbon (3.5) (2.5)



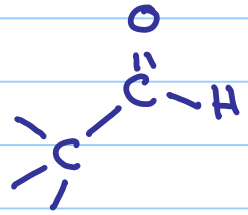
∴ Carbonyl Reactivity is one of....

A) 

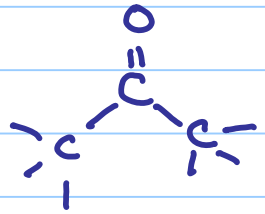
B) 

Main Carbonyl Functional Groups

I) Aldehyde Oxidation Level (2 Bonds to X)

a) 

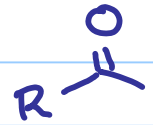
Aldehyde
- One H atom one C atom
('al' in Naming)

b) 

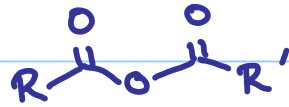
Ketone - Two C atoms attached
('one' in Naming)

Note: (imines 'C=N' Honourary member)

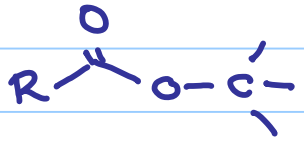
II Carboxylic Acid Oxidation Level
- 3 Bonds to X

a) 

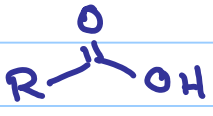
Acid Chloride (Acyl Chloride)
(one C atom, one Cl atom)

b) 

Anhydrides
(- one C atom, one 'O' of an "Ester")

c) 

Ester
(one C atom), one 'O' atom of an Ether)

d) 

Carboxylic Acid Acid
('O' Atom of Alcohol)

e)  AMIDE

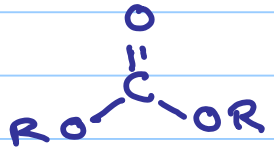
("N" ATOM ON CARBONYL)

R' CAN BE H OR C

(R-C≡N NITRILE/CYANIDE IS HONORARY MEMBER)

III CARBONATE OXIDATION LEVEL
(FOUR BONDS TO X ATOMS)

a) O=C=O CARBON DIOXIDE

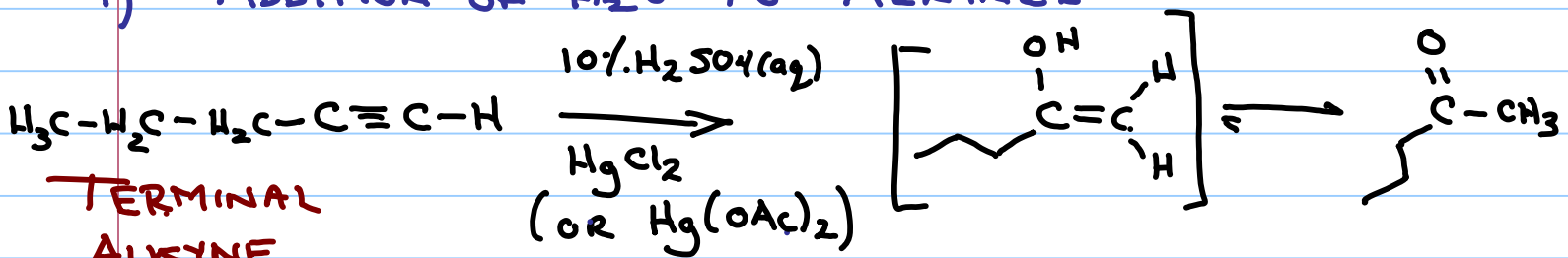
b)  CARBONATE

(CARBAMATES, UREAS ARE BEING IGNORED)

ALDEHYDE OXIDATION LEVEL CASES.

PREPARATIONS

1) ADDITION OF H_2O TO ALKYNES

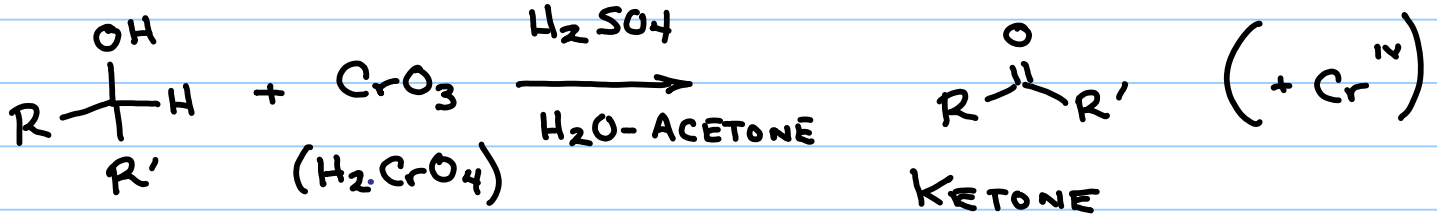


TERMINAL ALKYNE

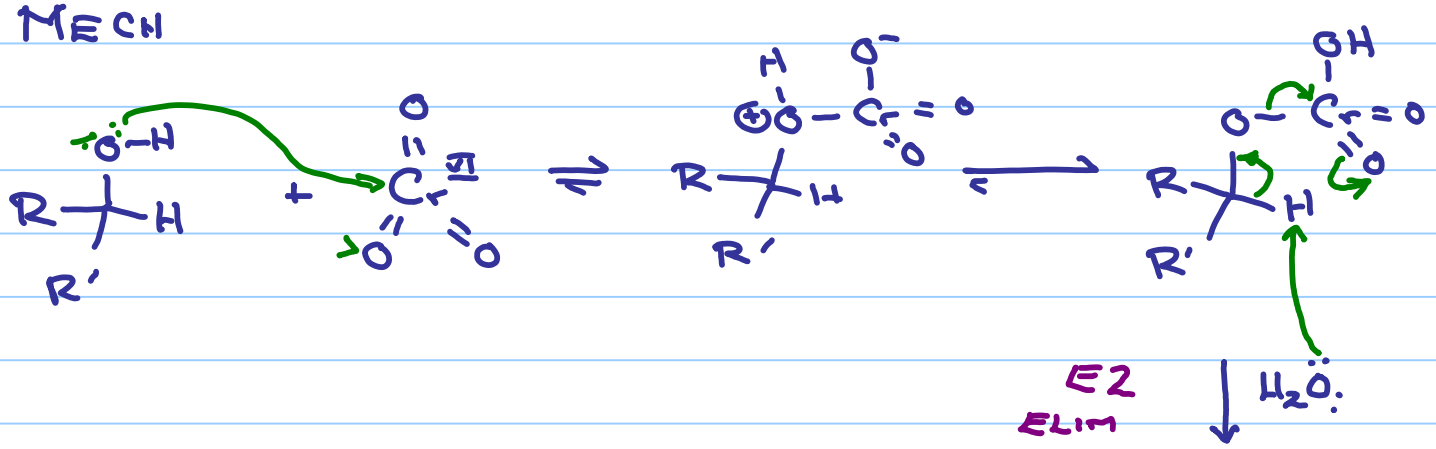
(MARKOVNIKOV ADDN)

19.6 ; 19.6a

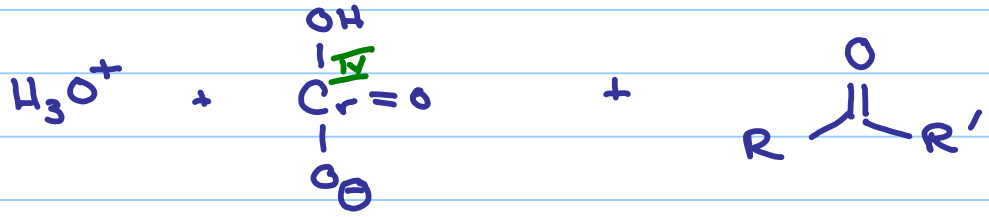
2) OXIDATION OF ALCOHOLS WITH Cr^{VI}

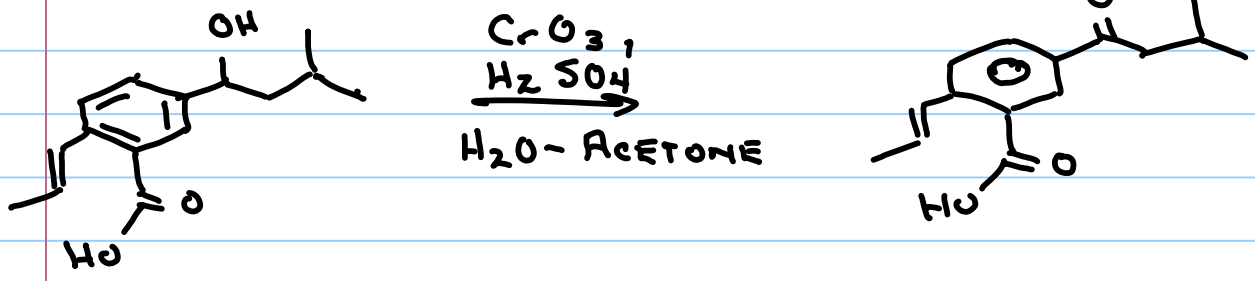


MECH



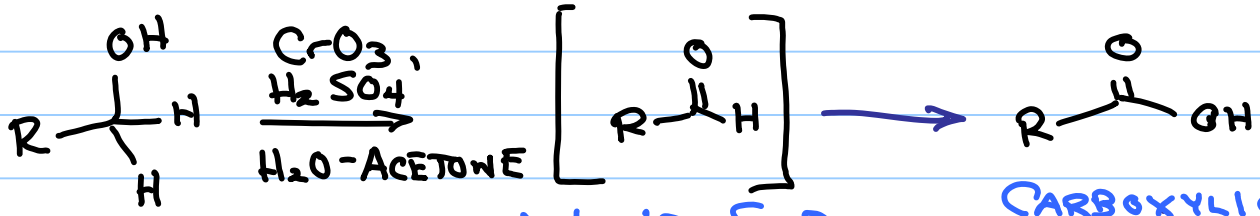
PROMISE TO TEST MECH. NOT





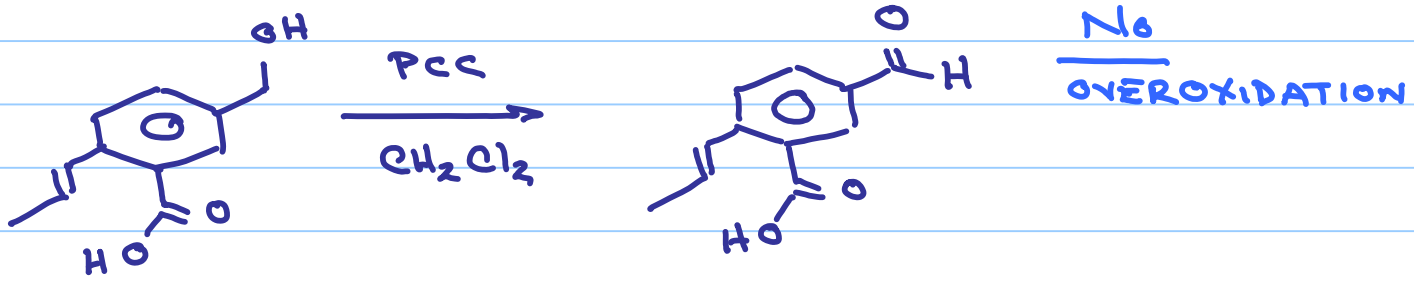
PROBLEM.

- FOR 1° ALCOHOLS, RXN DOESN'T STOP AT ALDEHYDE



SOLUTION – ADD PYRIDINE TO SCAVENGE H^+

PYRIDINIUM CHLOROCHROMATE (PCC)



(NOTE: PCC WORKS FOR 2° ALCOHOL TO KETONE OXIDATIONS)

REACTIONS OF ALDS / KETONES WITH NUCLEOPHILES

i) WITH OXYGEN BASED NUCLEOPHILES

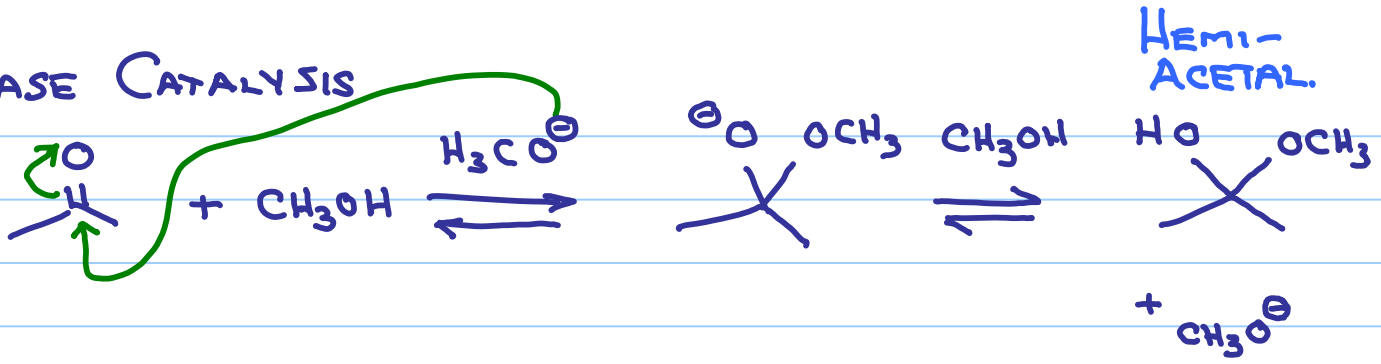
ii) WITH CARBON BASED NUCLEOPHILES
HYDRIDE (H^-) NUCLEOPHILES

i) OXYGEN NUCLEOPHILES.

– $H_2\ddot{O}$, $CH_3\ddot{O}H$, $R\ddot{O}H$

– REACTION IS INCREDIBLY SLOW
– MUST ADD BASE OR ACID CATALYST

BASE CATALYSIS

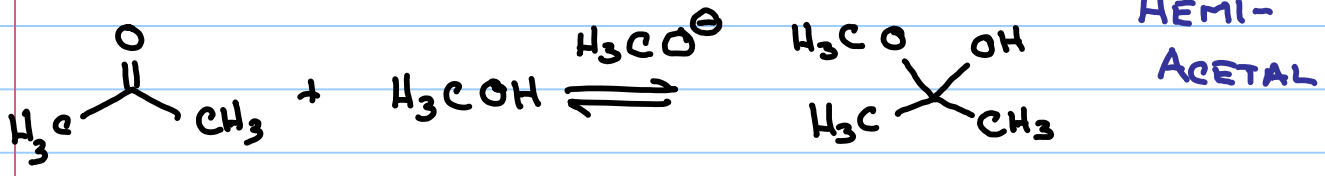


HEMI-ACETAL.

Lecture 14

Note Title 3/2/2017

Oxygen Based Nu⁻'s.

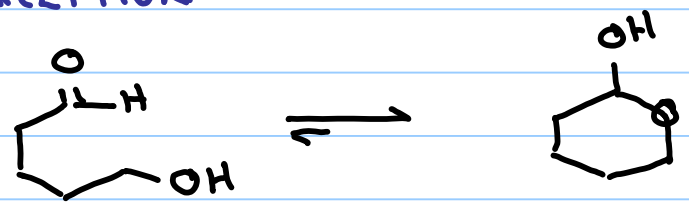


Hemi-Acetal

- One Big Problem $K_{eqm} << 1$ For 95% of Aldehydes + Ketones

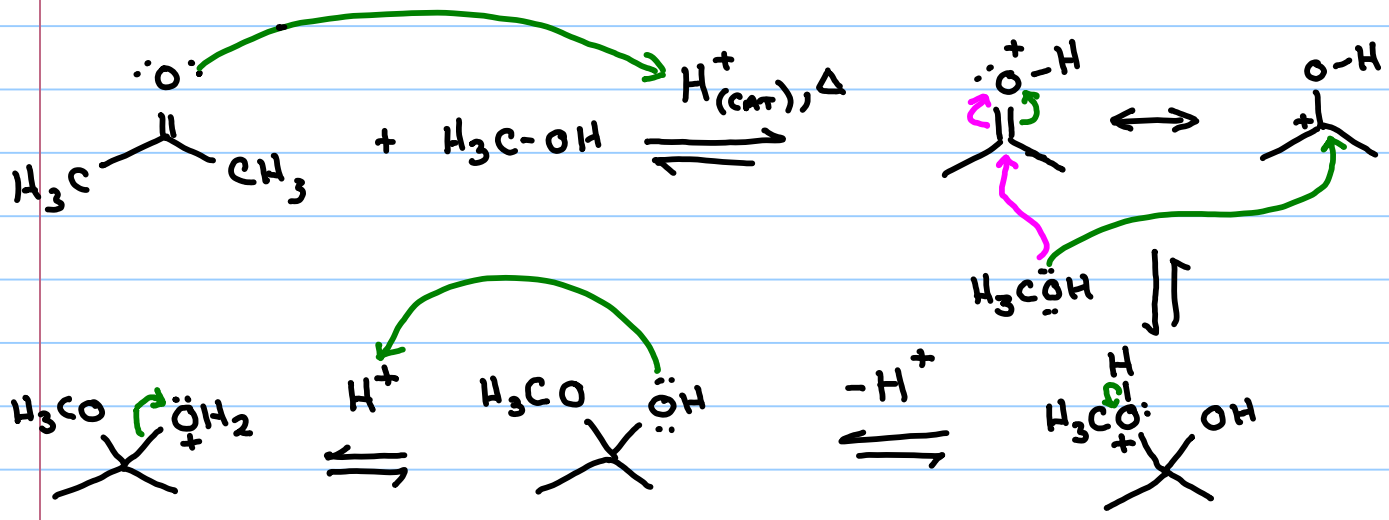
∴ No useful Synthetic Result

Exception



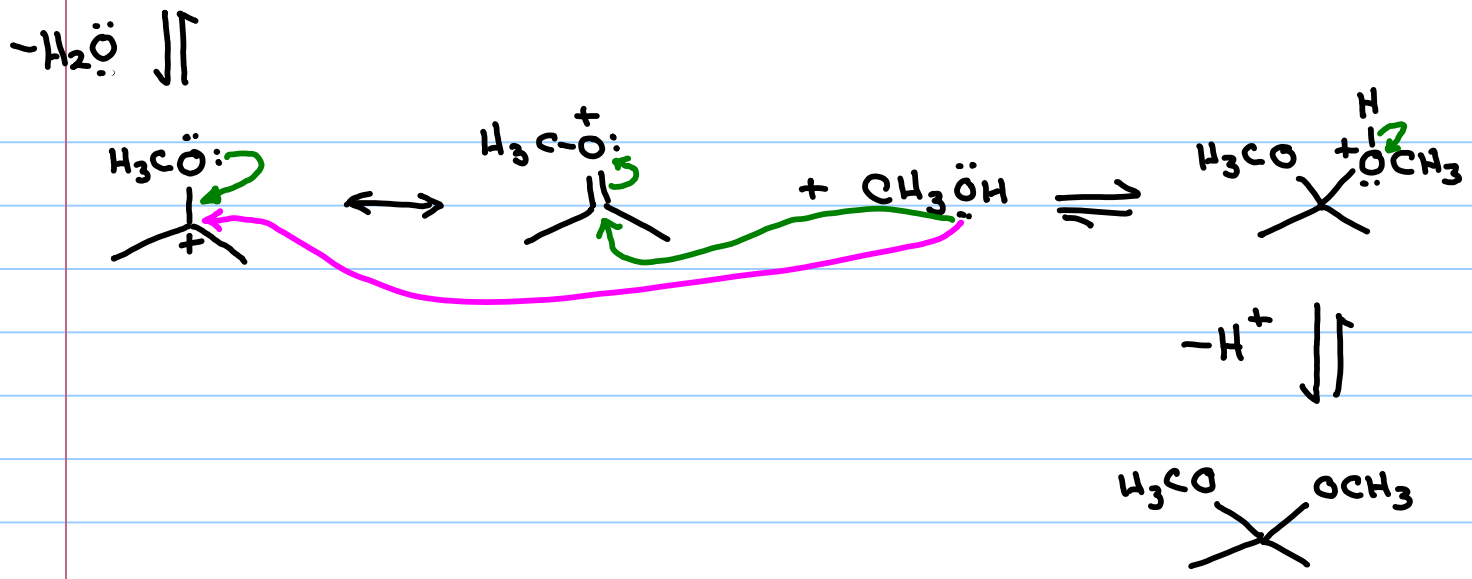
5- or 6-memb. Ring Furanose + Pyranose Form of Sugars

Acid Catalysis - Quite Different, Get a Real Synthetic Result



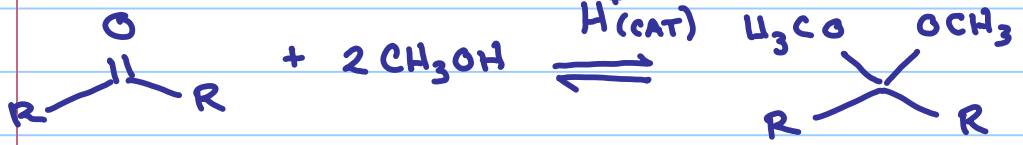
Rxn Can Go Further

therefore, it doesn' stop at hemi-acetal



ACETAL

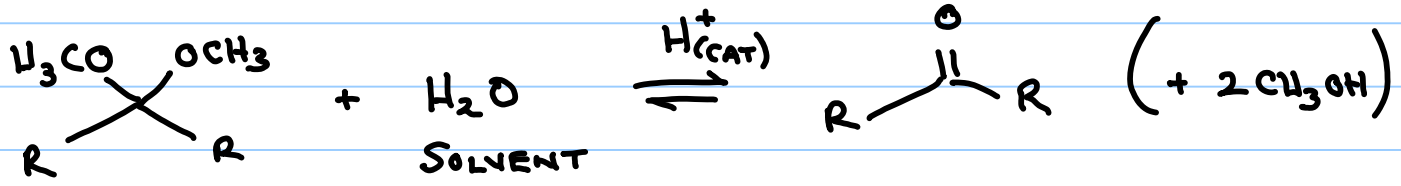
OVERALL



- CAN GET GOOD YIELDS OF ACETAL BY USING CH_3OH AS SOLVENT, OR
- BY REMOVING WATER AS IT IS FORMED (DEAN-STARK TRAP)

- ACETALS ARE V. USEFUL - STABLE, STORABLE CPDS
  - TEMPORARILY CAN BE USED TO "PROTECT" AN ALDEHYDE OR KETONE FROM CHEMICALS THAT REACT WITH IT (GRIGNARD REAGENTS, HYDRIDES, BASES, OTHER REDUCTIONS)

- TO MAKE RXN REVERSE

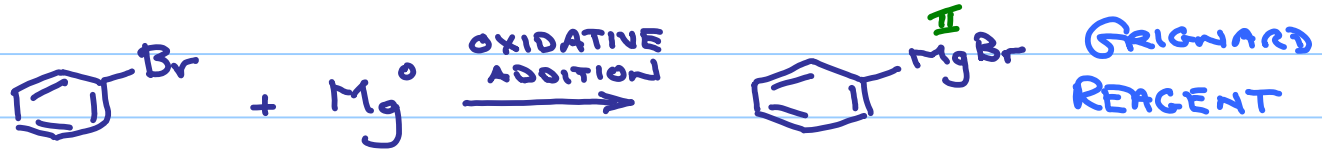


17.5 KARTY

CARBON NUCLEOPHILES (STRONG $Nu^{\ominus}$)

EQUIVALENTS OF $-C^{\ominus}$

GRIGNARD REAGENTS (ORGANOMAGNESIUM CPDS)



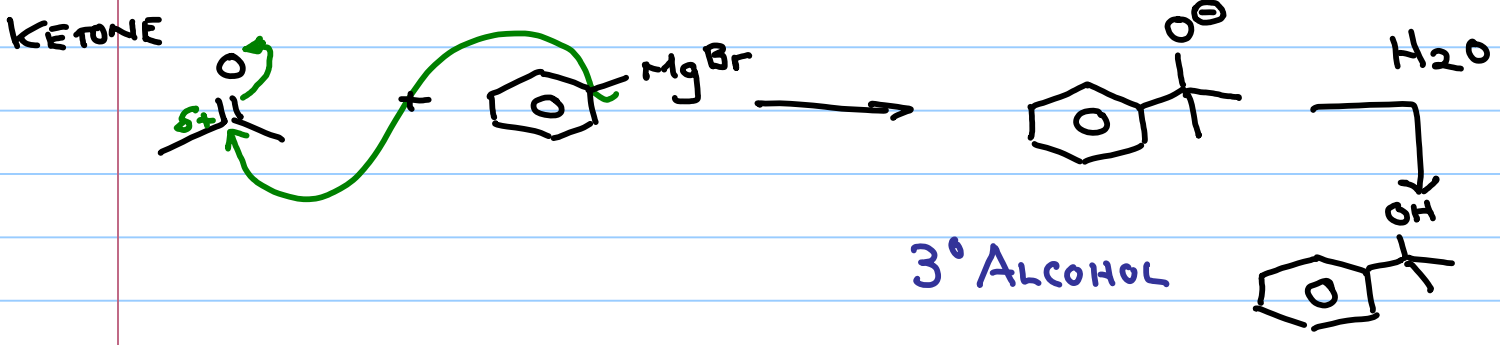
- CAN USE ORGANIC IODIDES OR CHLORIDES INSTEAD
  - BROMIDES MOST COMMON

- C-Mg BOND IS REALLY VERY POLAR COVALENT, BUT I'M FINE WITH

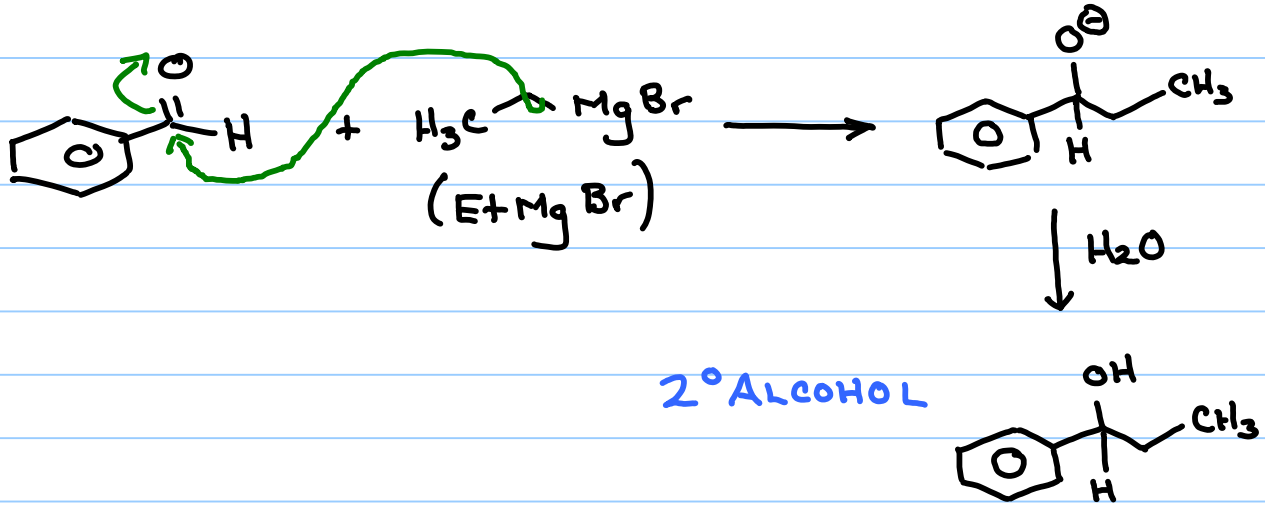
MORE REACTIVE THAN, BUT ANALOGOUS TO GRIGNARD REAGENTS

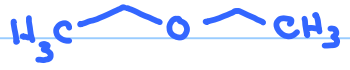
- VERY REACTIVE – DON'T SUBJECT TO H_2O, ROH, RSH, OR NNH_2, OR ELSE

REACT IMMEDIATELY WITH ALDEHYDES AND KETONES



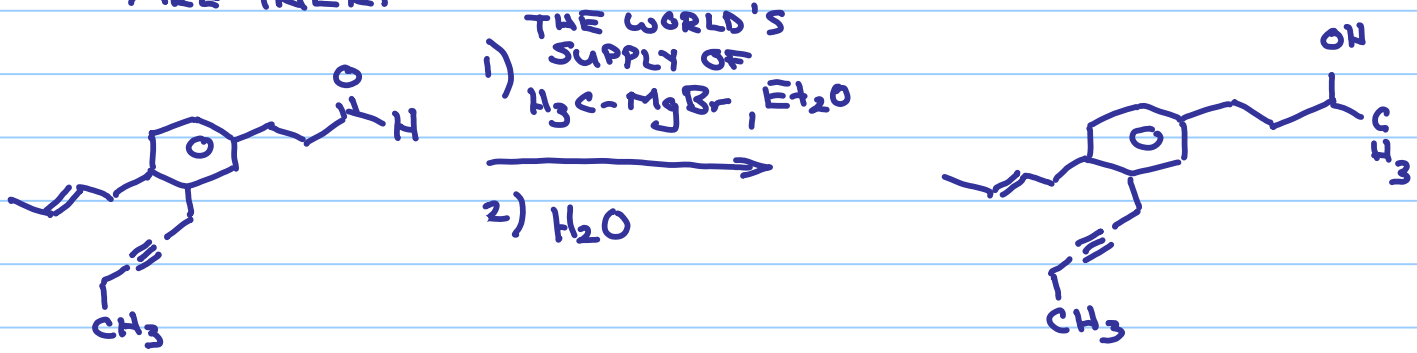
ALDEHYDES - SLIGHTLY MORE REACTIVE THAN KETONE, OTHERWISE THE SAME



- SOLVENT ? ETHERS  DIETHYL ETHER (Et_2O)

 TETRAHYDROFURAN (THF)

- NEED A POLARIZED MULTIPLE BOND TO REACT
  ∴ MOST ALKENES, MOST ALKYNES, BENZENES ARE INERT



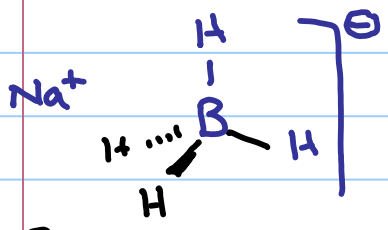
EXCEPTION

17.3 KARTY

Hydride ($H^{\ominus}$) Nucleophiles

- Obvious ones NaH or KH
  - Not Good Choices - Prefer to Act as Bases instead of Nucleophiles

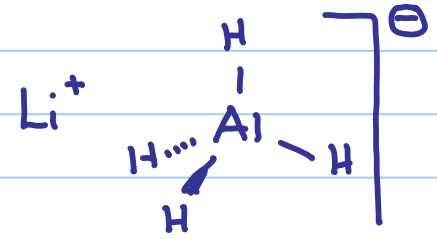
The Nucleophilic Ones are .....



Sodium Borohydride

$NaBH_4$

- Gentle, Milder
- Can use an Alcohol Solvent
- Even H_2O
- Reacts w Aldehydes, Ketones + Little Else

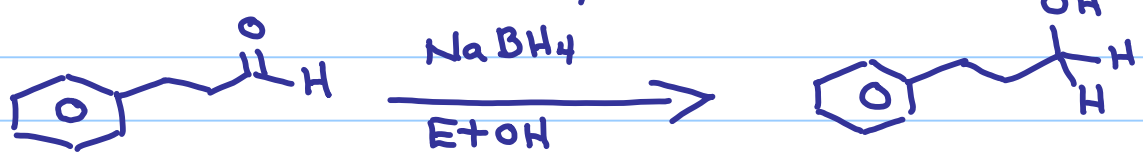


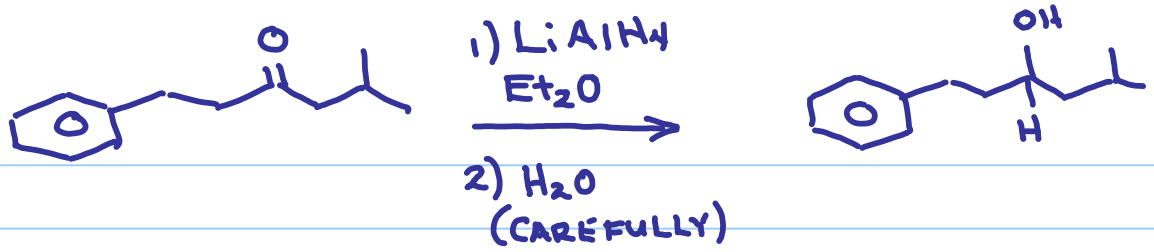
Lithium Aluminum Hydride

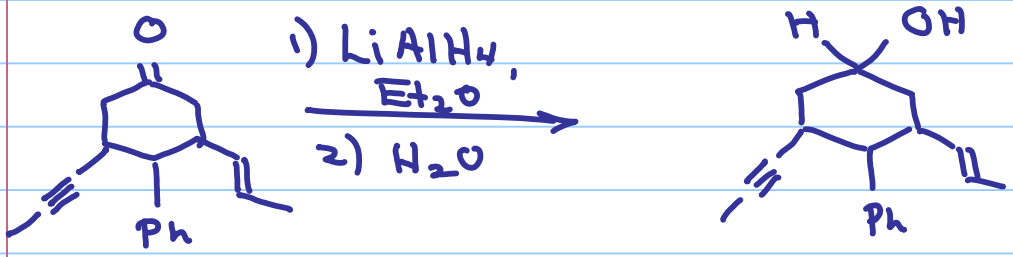
$LiAlH_4$

- Very Vigorous
- No OH's Please or Else Poof!
- Et_2O, THF Solvent
- Reacts with All Carbonyls

- Rxns w Aldehydes, Ketones





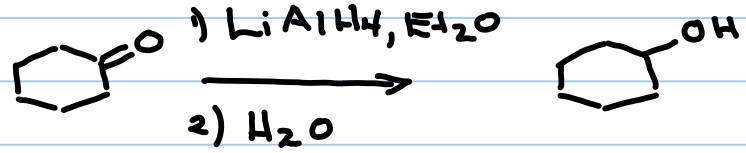


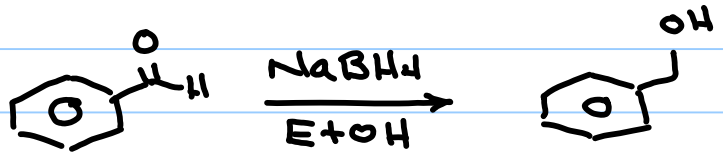
NON-POLARIZED C≡C BONDS ARE NORMALLY INERT

LECTURE 15

Note Title 3/7/2017

WHERE WE LEFT OFF



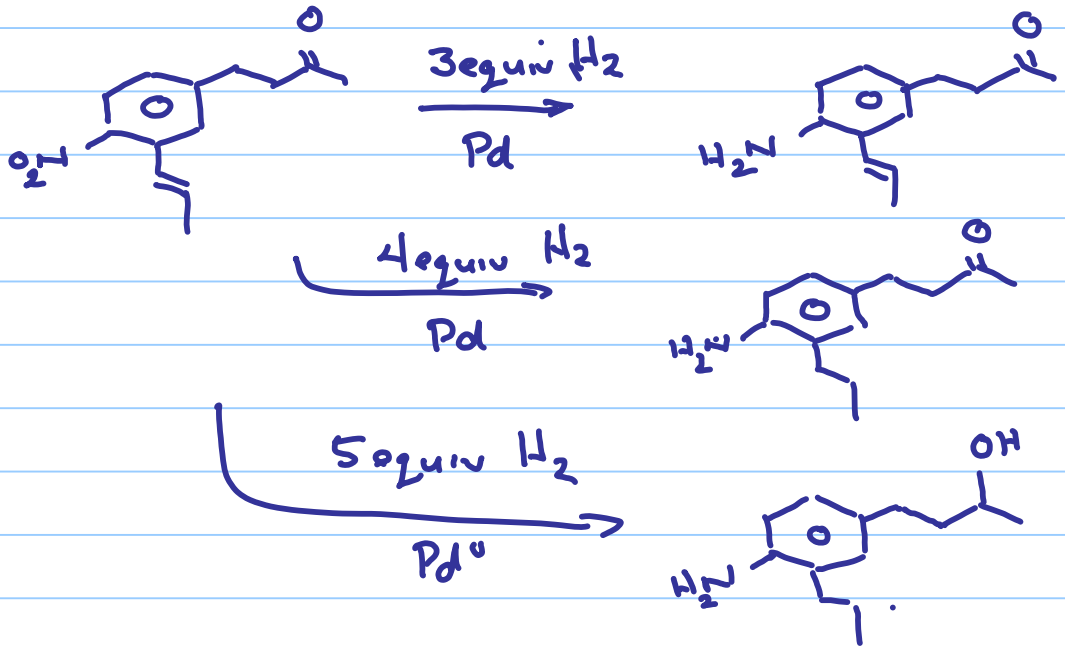


WHY NOT H_2 + CATALYST (i.e. Pd°, Ni)

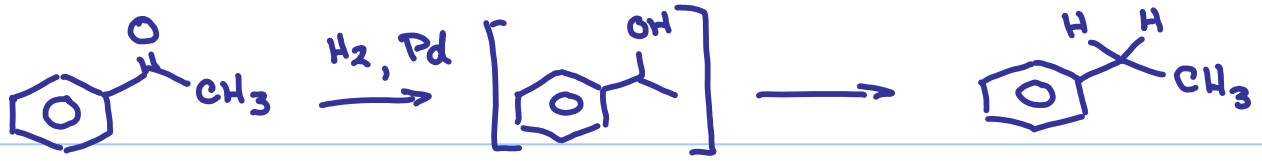
- THIS SET OF REAGENT WILL REDUCE ALDEHYDES & KETONES, BUT.....

ISSUE #1 - OTHER THINGS ARE REDUCED 1ST

- NO_2 > $-C\equiv C-$ > $'C=C'$ > $'C=O$

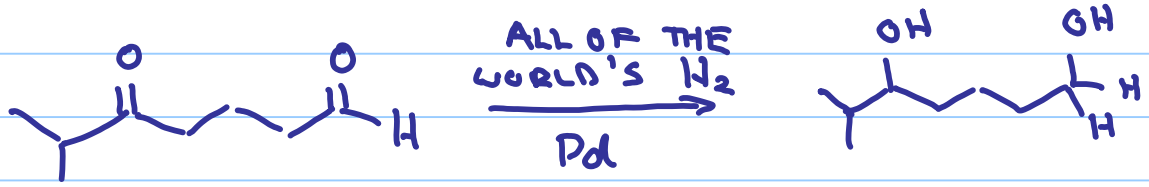


ISSUE #2 - ARYL KETONES, ALDEHYDES GO A BIT DIFFERENTLY



DOESN'T STOP HERE

ALKYL KETONE / ALDEHYDE



CARBOXYLIC ACID GROUP OF CARBONYLS

ACID CHLORIDE | ANHYDRIDE | ESTERS | ACIDS | AMIDES

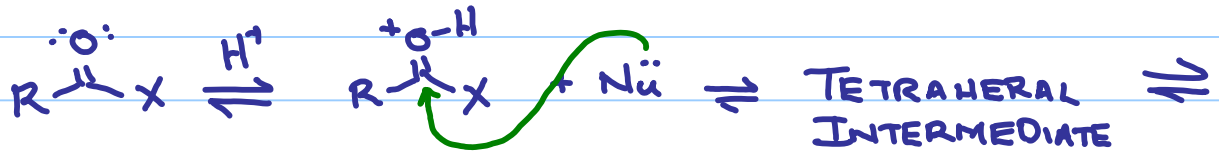
REACTIVITY - MUCH IN COMMON

TETRAHEDRAL INTERMEDIATE - TRANSIENT

- REACTIVITY AT 'ACYL' CARBON IS ENHANCE RELATIVE TO ALKYL ANALOGUES

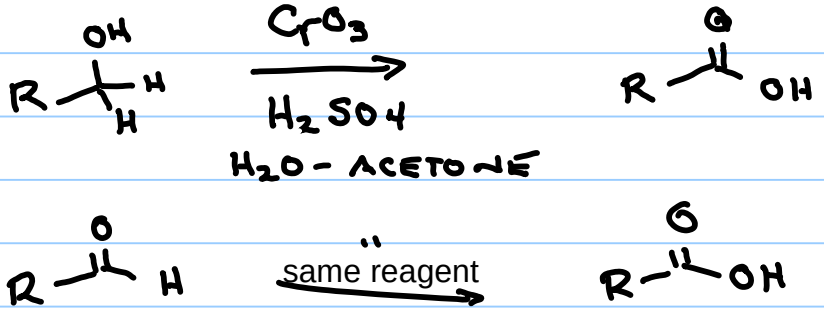
∴ ACID CHLORIDES - VERY, VERY REACTIVE
ANHYDRIDES - VERY REACTIVE
ESTERS - REACTIVE
AMIDE - SLUGGISH BUT DOABLE

- NUCLEOPHILES DOESN'T HAVE TO BE CHARGED, USUALLY BECAUSE WE CAN DO ACID CATALYSIS

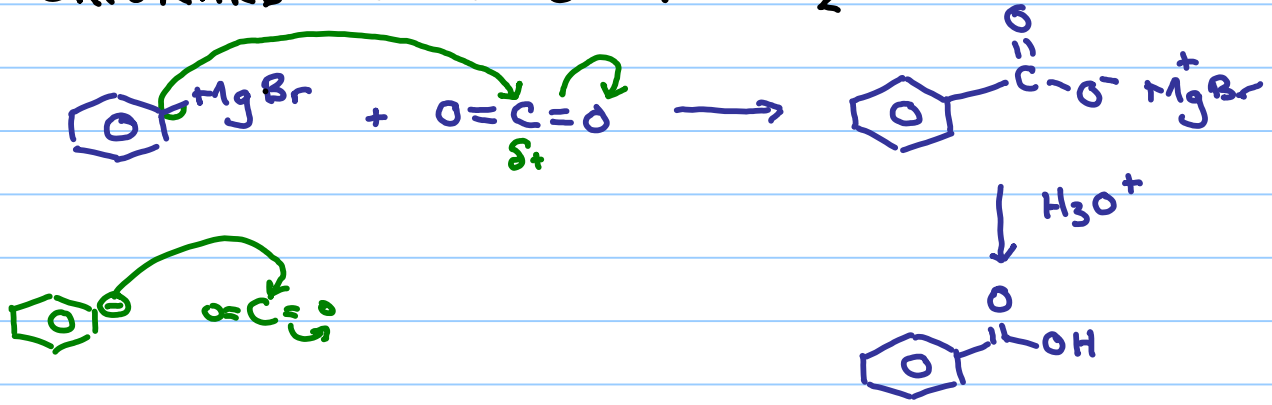


PREPARATIONS OF ACIDS

1) OXIDATION

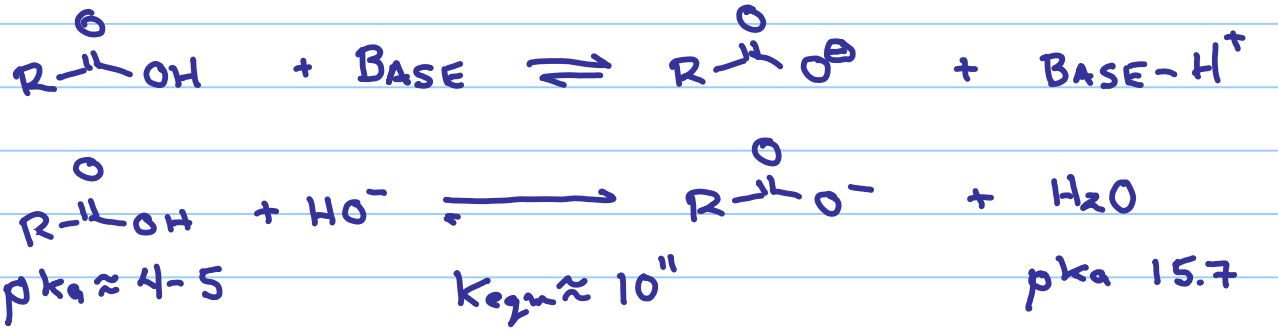


2) GRIGNARD REAGENTS + CO_2



CARBOXYLIC ACIDS- PROPERTIES

#1 & MAJOR - THEY'RE ACIDIC



KARTY - CH 20, 21

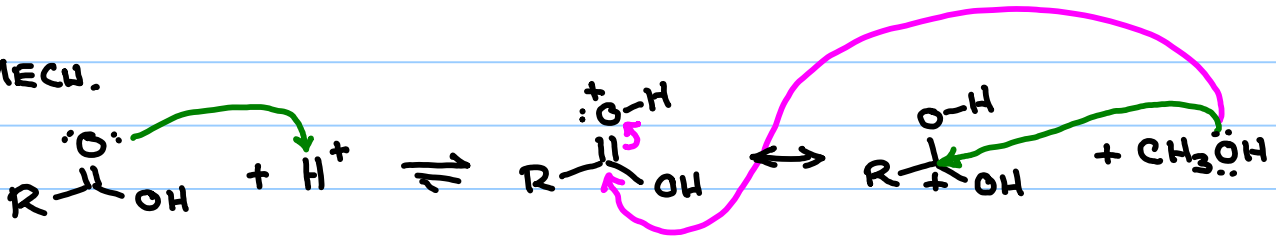
RXNS - CARBOXYLIC ACIDS.

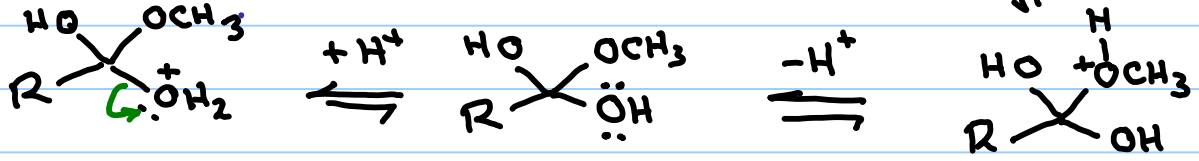
- OXYGEN NUCLEOPHILES

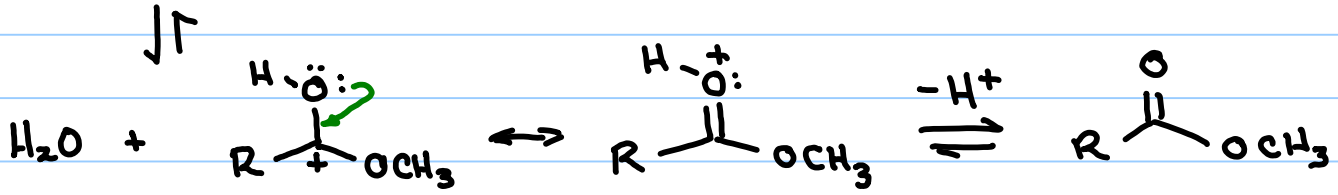
BASE INDUCED. - NOTHING REALLY

ACID CATALYZED - ABSOLUTELY

MECH.





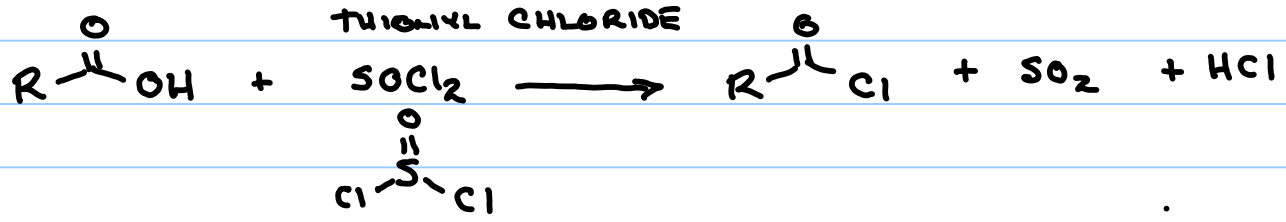


RXN IS AN EQUILIBRIUM

- GET RXN TO COMPLETION BY USING ALCOHOL AS SOLVENT

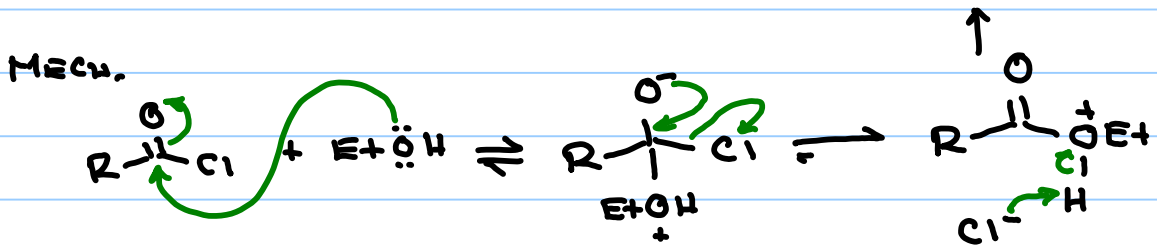
- CAN ALSO MAKE ACID FROM ESTER (REVERSE RXN) JUST BY USING H_2O AS SOLVENT

Alternative - Use Acid Chlorides

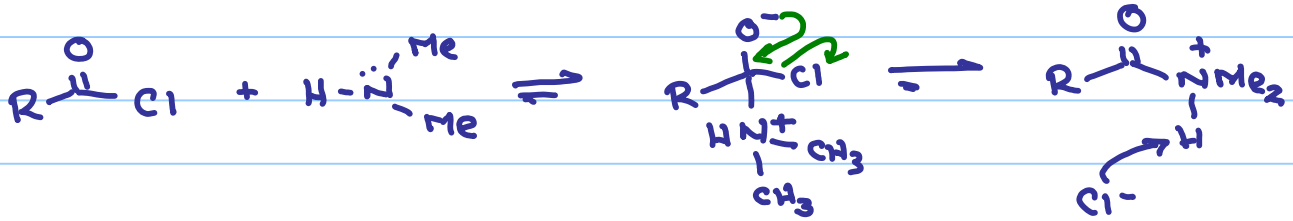


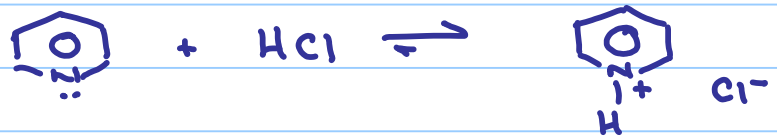
Very, Very Reactive – Don't Need any Catalyst

– Don't Survive H_2O



Acid Chloride ⊕ Amines ⟶ Amides



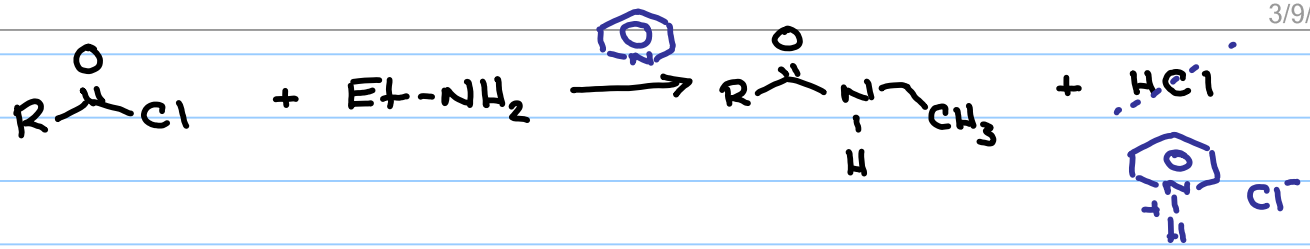


TEST #2 THURS MAR. 16 10-11 am

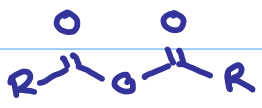
A-L 1120 ERIE M-Z HERE (200 TOLDO)

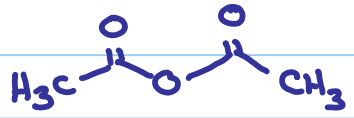
Lecture 16

Note Title 3/9/2017

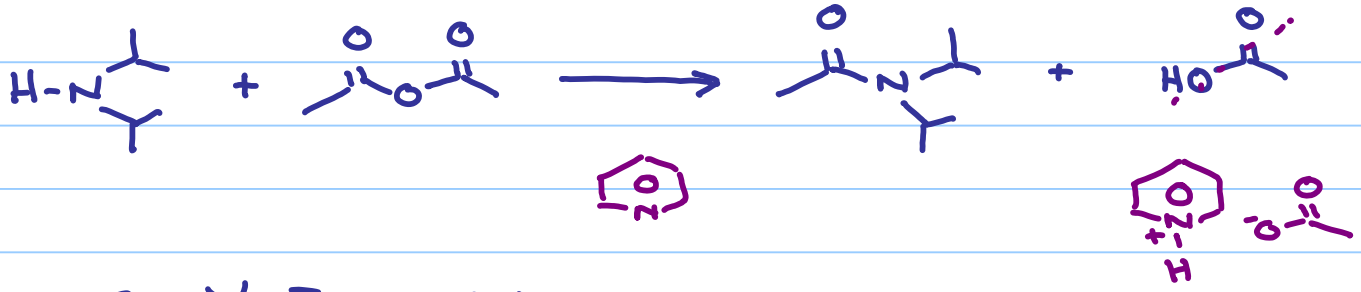


Anhydrides

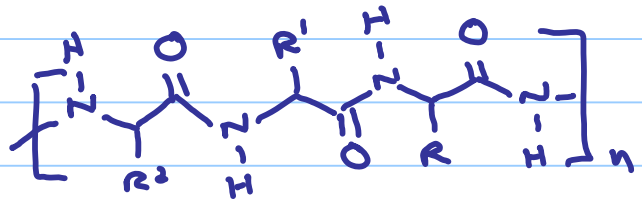
- 
- 2nd in Reactivity
- R's usually the same, but don't have to be



Acetic Anhydride

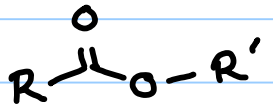


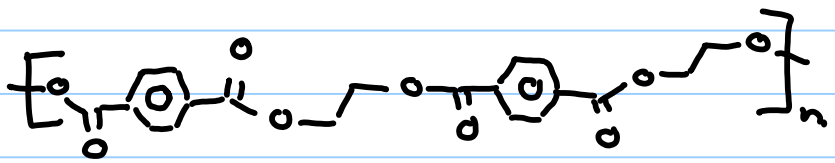
Amides - V. Important



Proteins

(Carboxylic) Esters





Polyethylene Terephthalate

'Polyester'

Reactions w/ Nucleophiles

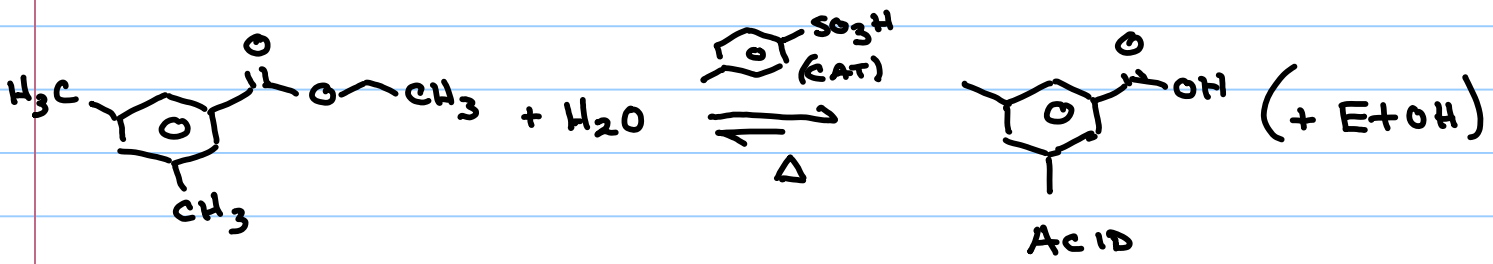
1) Oxygen Nucleophiles

- Acid and Base Catalyzed Rxns <u>Both</u> now work

a) Acid

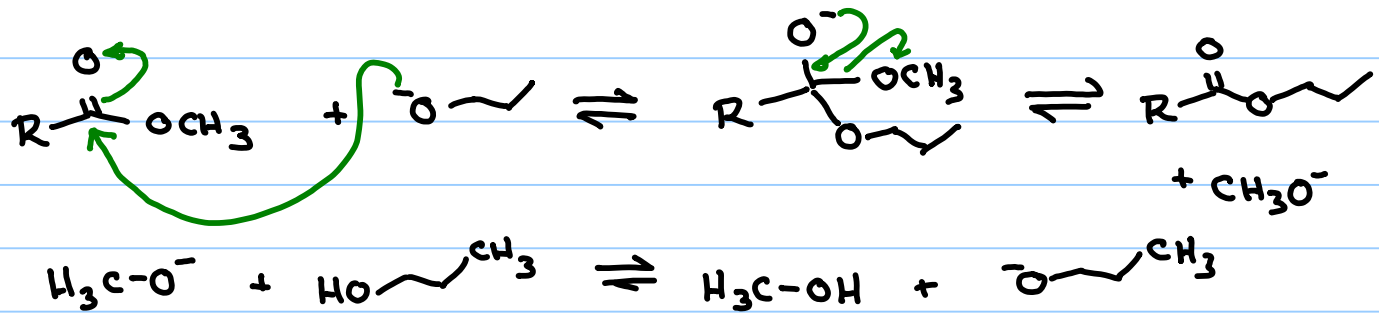
- Force Rxn to Product Side by using Excess Alcohol (in this case H_3C—OH)

If H_2O instead

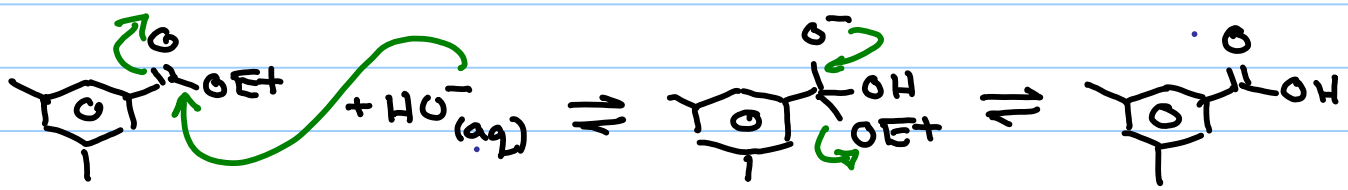


b) Base Catalyzed ones now work nicely

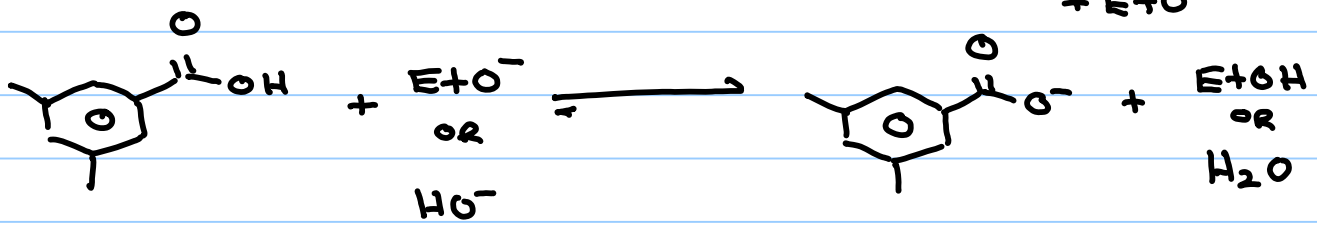
Mech.



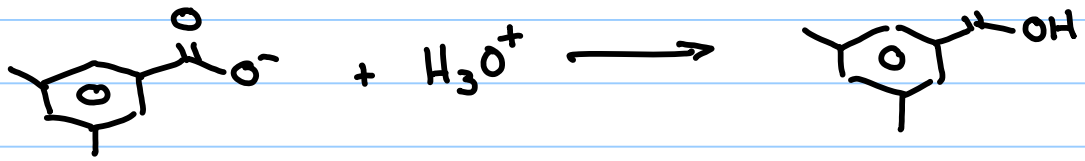
FOR MAKING CARBOXYLIC ACIDS, BASE IS ACTUALLY BETTER, ESPECIALLY IF YOU USE A LOT OF HO^- (I.E. NOT A CATALYTIC AMOUNT)



almost irrev. pushes rxn to completion



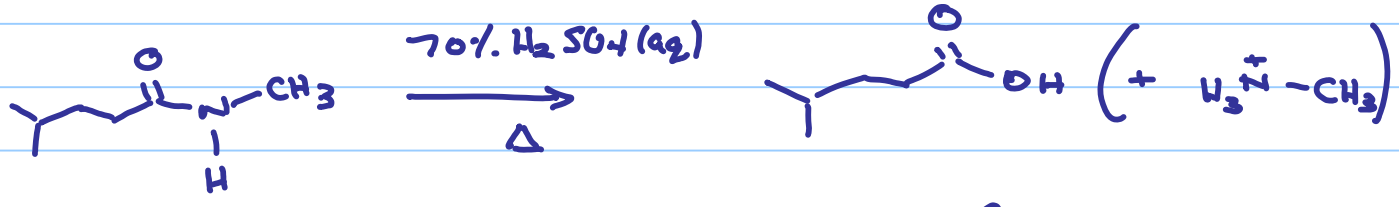
V. USEFUL - SAPONIFICATION AT THE END



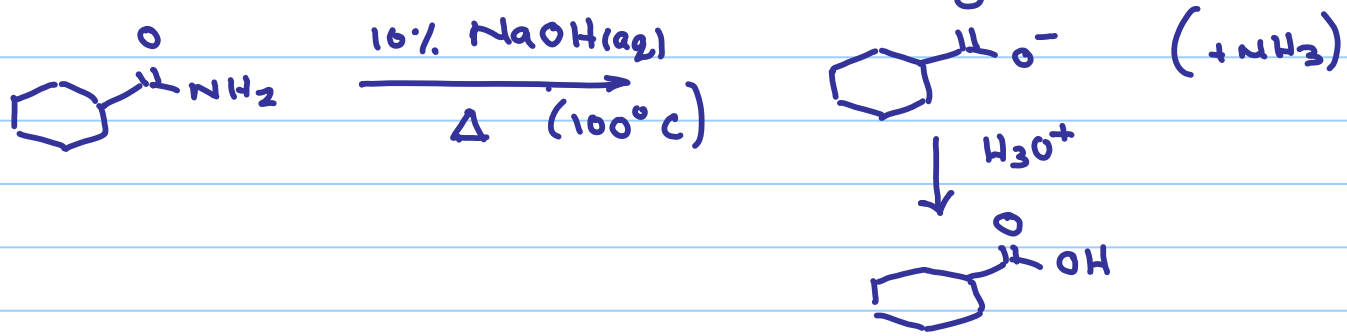
THE SAME REACTIONS FOR AMIDES ??

- YES, BOTH ACID AND BASE CATALYZED
- MORE FORCING CONDITIONS, SINCE AMIDES ARE LESS REACTIVE

ACID

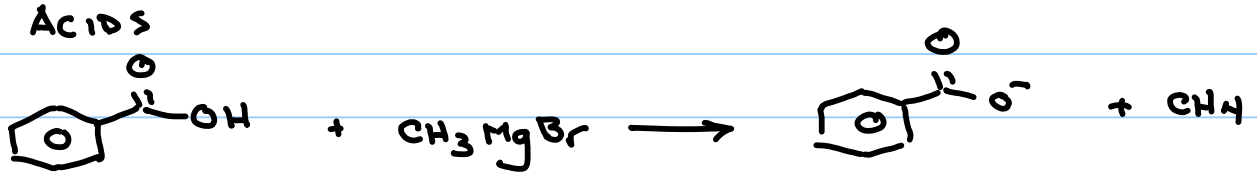


BASE



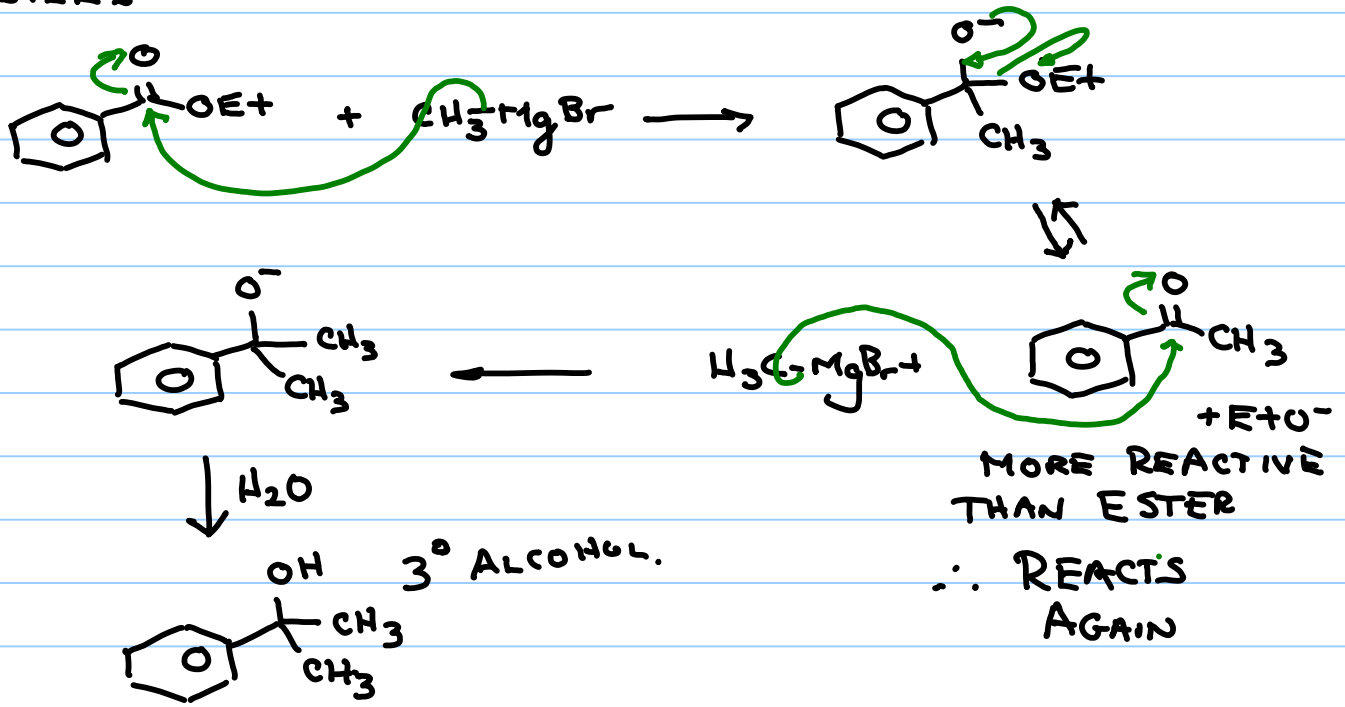
2) CARBON NUCLEOPHILES $R\text{-}MgBr \leftrightarrow R^{\ominus}\ {}^{\oplus}MgBr$

WITH ACIDS

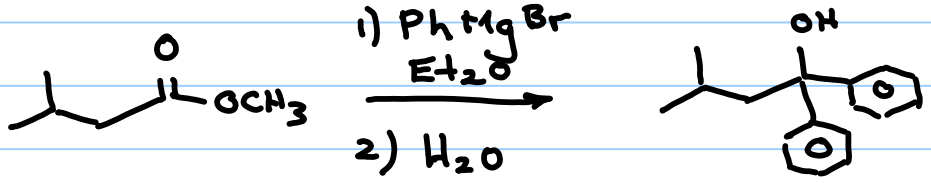


NOTHING 'PRODUCTIVE'

ESTERS



∴ GET 2 ADDNS OF GRIGNARD TO GIVE 3° ALCOHOL



HYDRIDES

$NaBH_4$

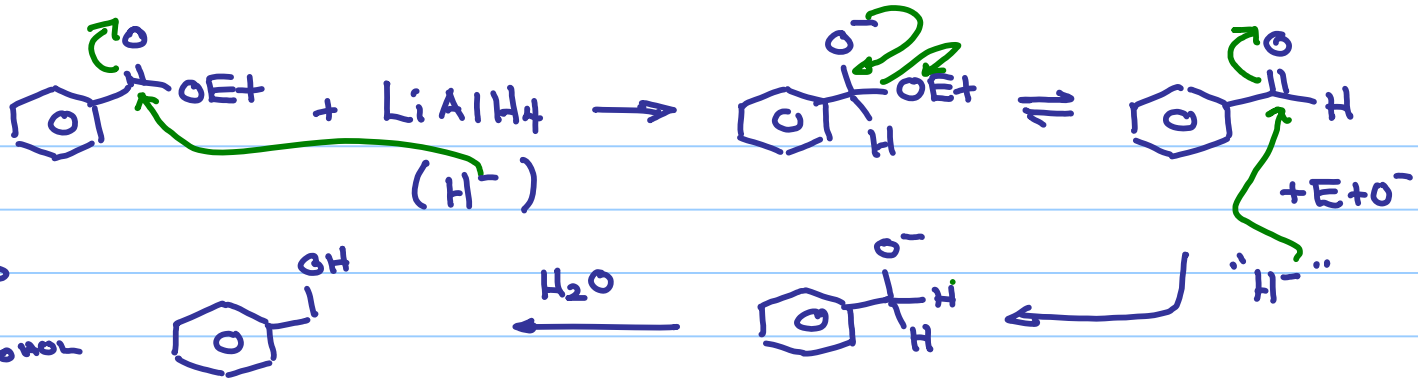
GENTLE

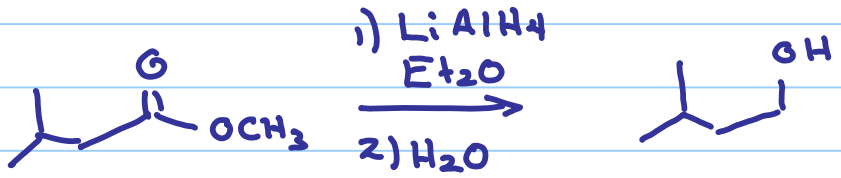
NO RXN

$LiAlH_4$

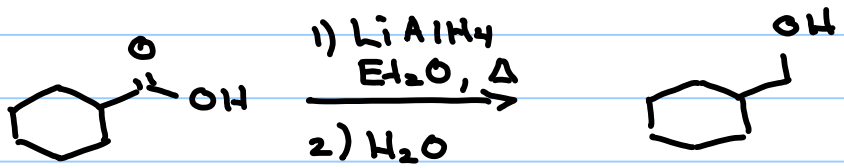
NOT AT ALL GENTLE

REACTIVE ENOUGH





IN FACT Li AlH4



WITH JUST A TOUCH OF WARMING, EVEN CARBOXYLIC ACIDS WILL REDUCE

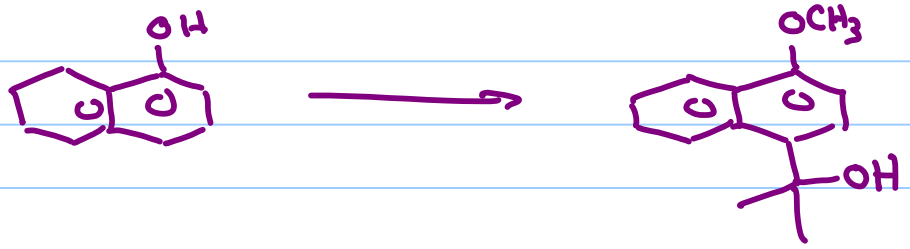
END OF TEST #2 MATERIAL

TEST #2 THURS. MAR. 16

10 AM – 11 AM.

A-L 1120 ERIE

M-Z HERE (200 TOLDO)



LECTURE 17

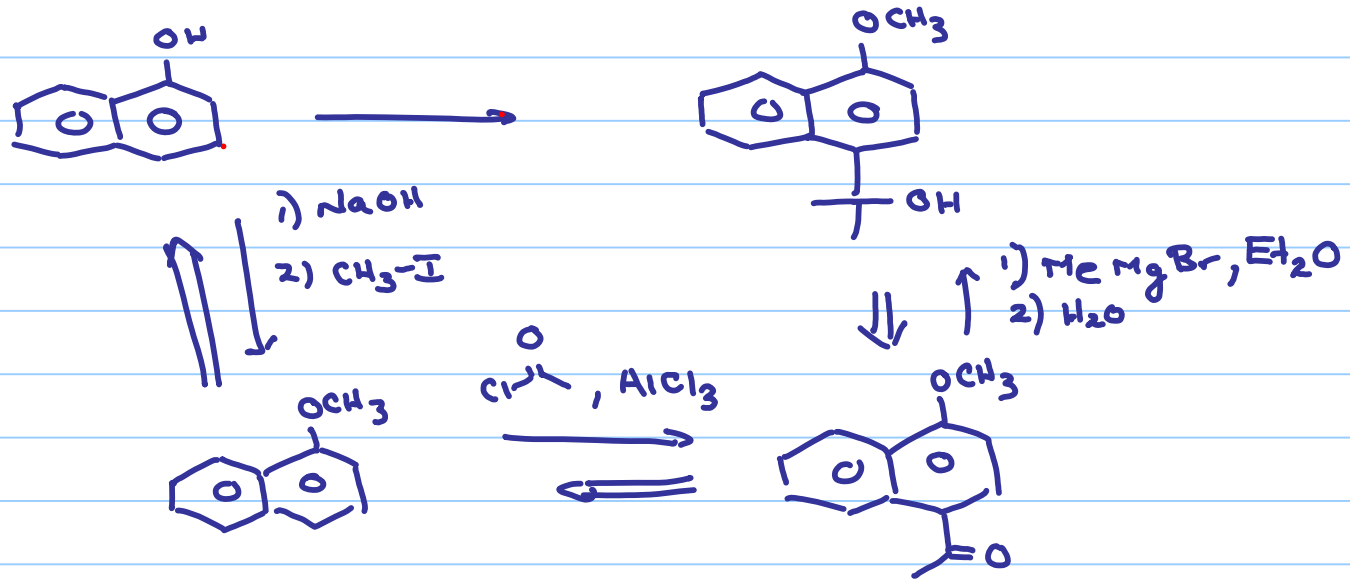
Note Title 3/14/2017

MIDTERM #2 THURS MAR 16

10 – 11 AM

M-Z HERE (TOLDO 200)

A-L 1120 ERIE



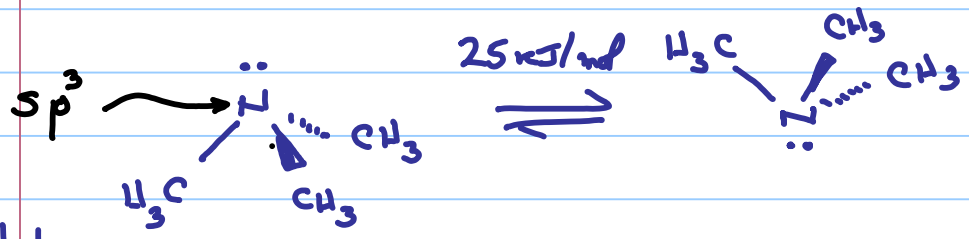
AMINES

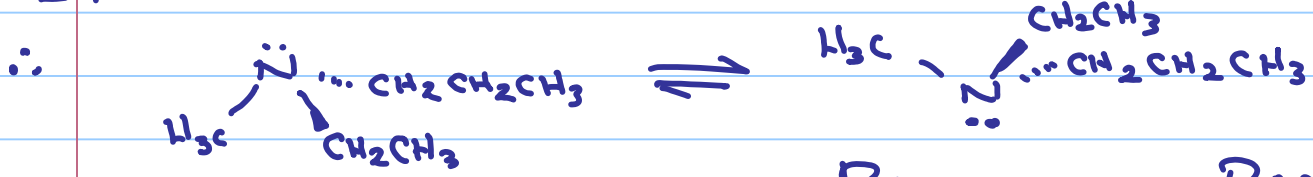
DERIVATIVES OF :NH_3 AMMONIA

$H_2\ddot{N}$-CH_3 — 1° AMINES

$H\ddot{N}(CH_3)_2$ — 2° AMINES

$\ddot{N}(CH_3)_3$ — 3° AMINES





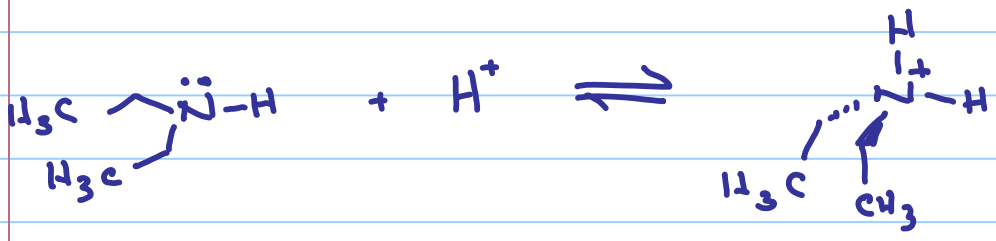
RACEMIZATION RAPID

∴ USUALLY NO CHIRALITY TO SPEAK OF AT N

#1. Very willing to share lone pair of electrons.

∴ Amines are Basic

∴ Amines are Decent Nucleophiles



pKa 9-11

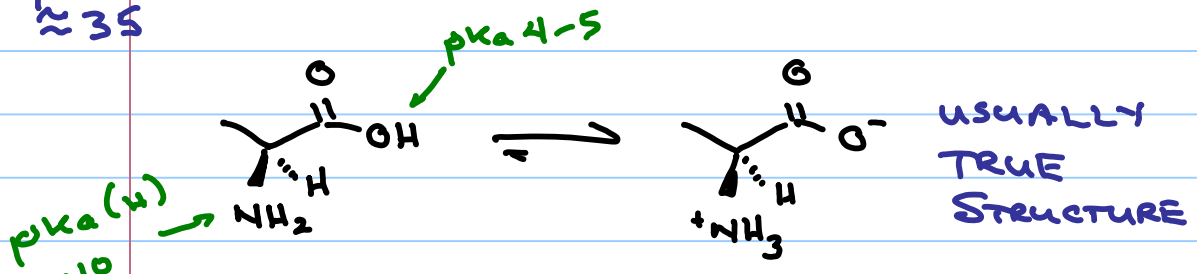
NH_3 9.26 Et_2NH 10.98 pKaH

Lower  4.6  5.3

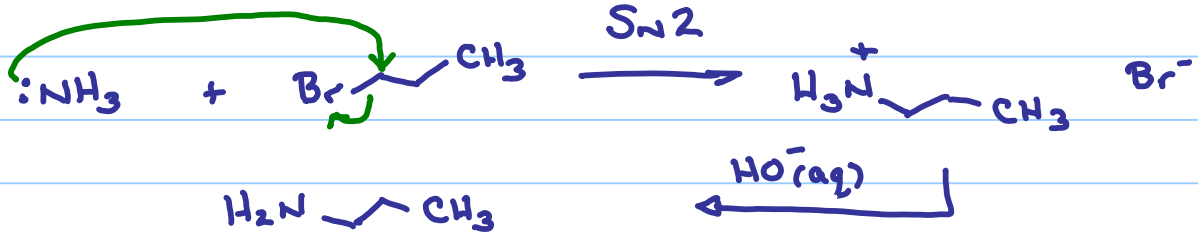
These are what are usually being referred to by the term "amine pKa", although pKaH is technically proper.

Keep in mind. Amines with N-H's do have *another* pKa that is occasionally relevant....

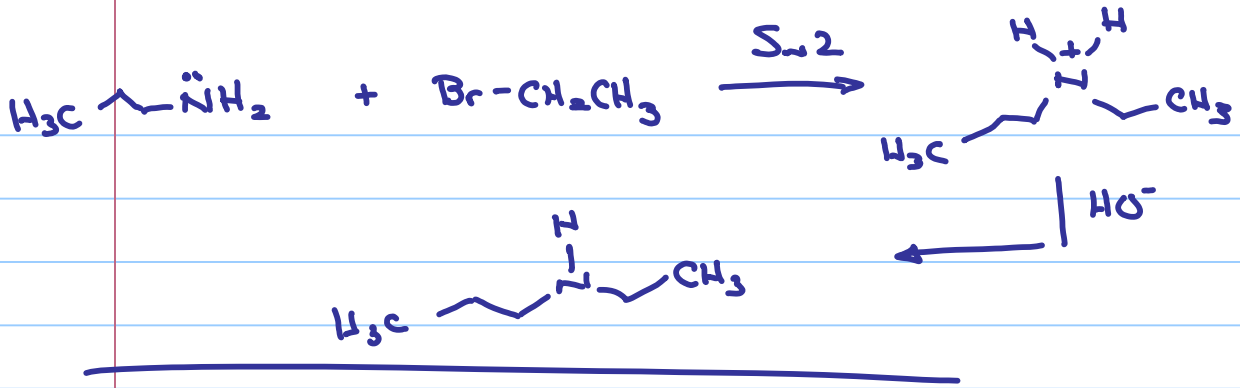
pKa ≈ 35 $NH_3 + H_2O \rightleftharpoons \bar{N}H_2 + H_3O^+$ NOTE: THERE IS A 2ND pKa

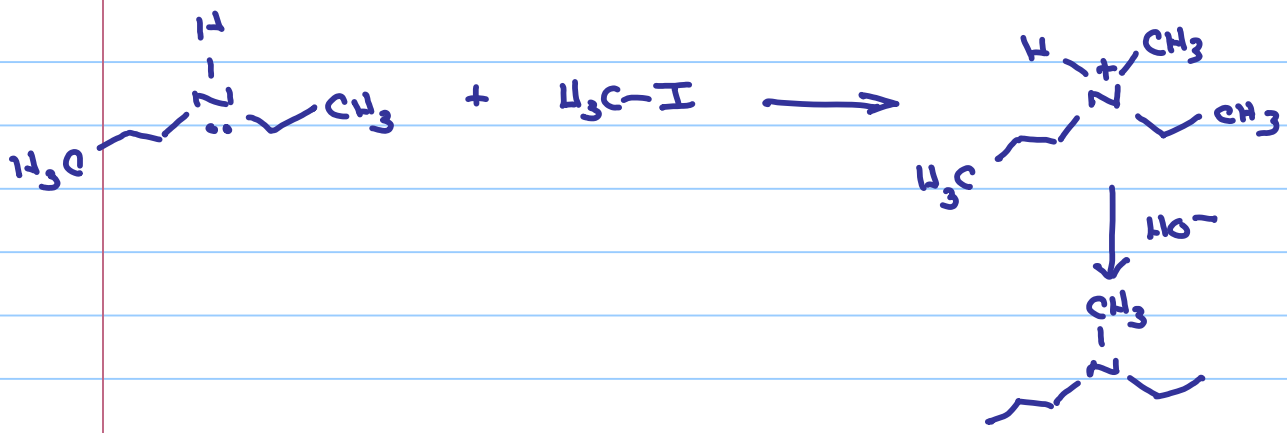


Nucleophilicity

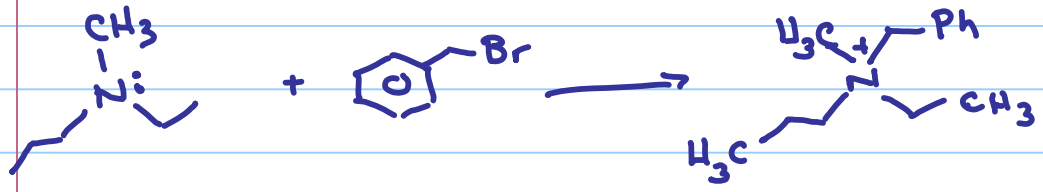


Simplest amine synthesis





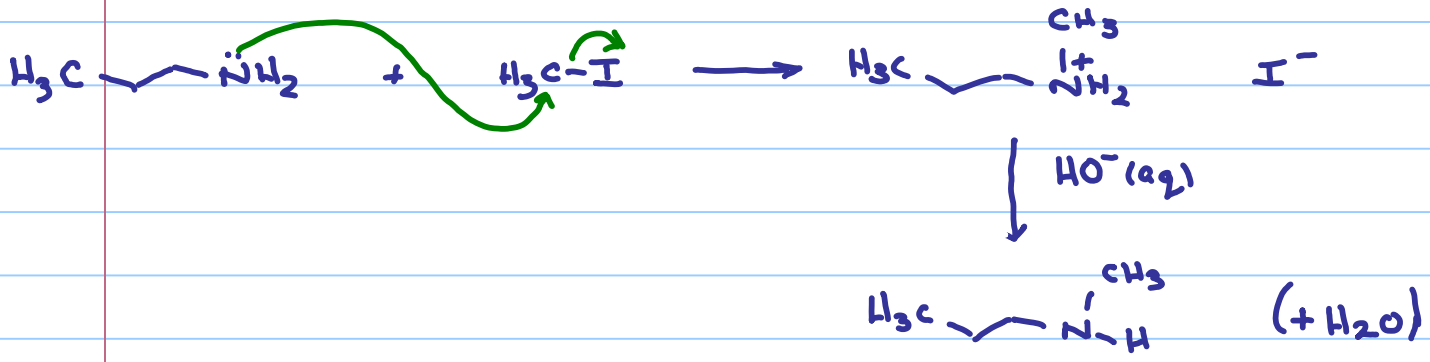
WILL ALKYLATE 3° AMINE TO GIVE 4° AMMONIUM SALT



Lecture 18

Note Title 3/21/2017

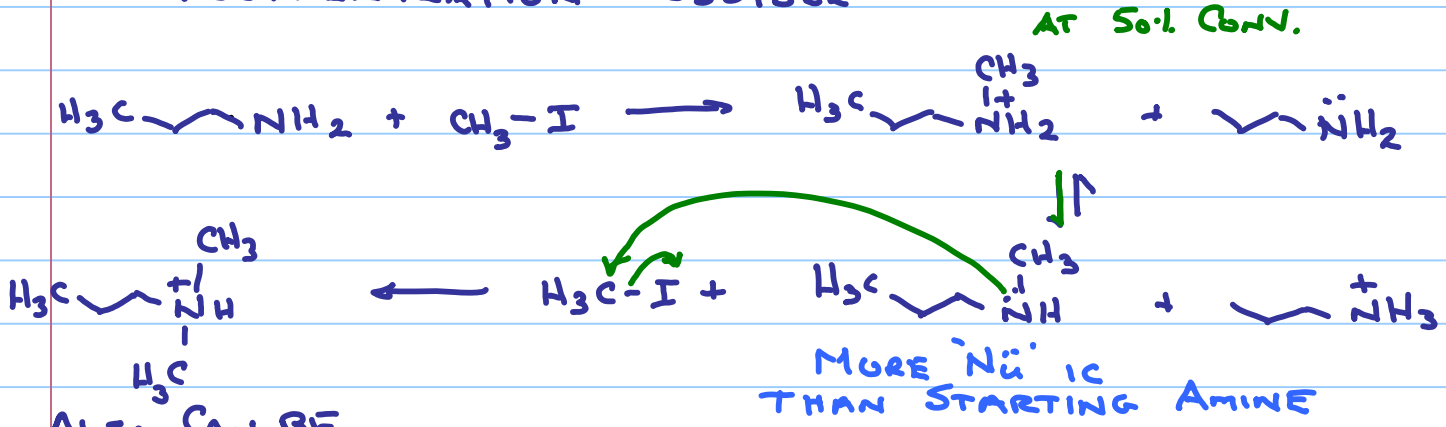
Amine Synthesis

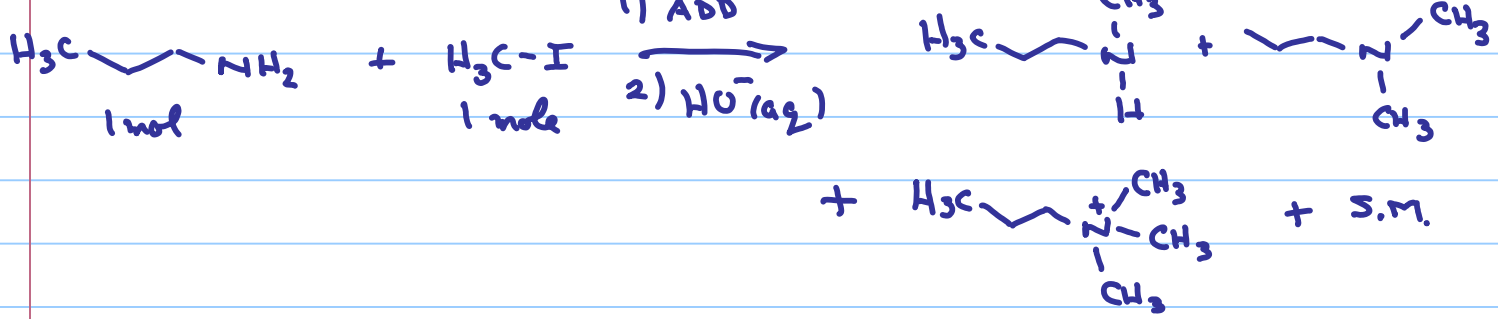


Problem

- Amines are Bases
- Alkyl Groups are Donating Groups (EDG)

∴ Polyalkylation Possible

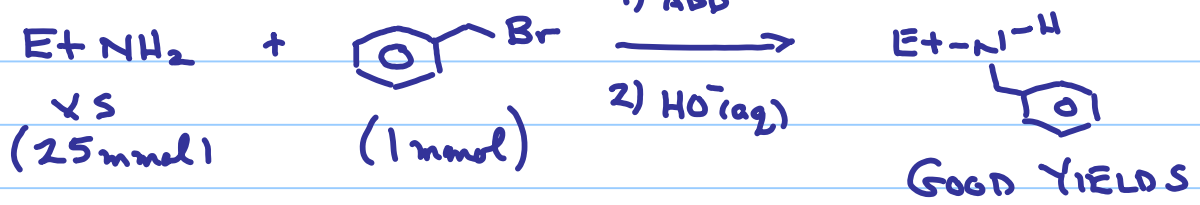




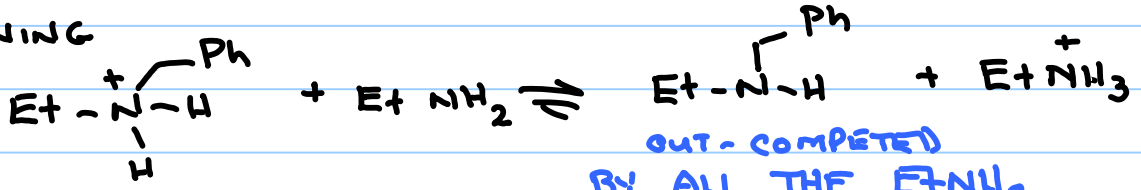
To Get Around this Polyalkylation Issue

1) Excess Amine

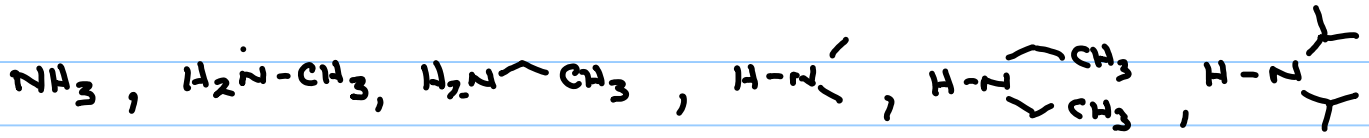
- Yes Alkylamines are more Nucleophilic than Ammonia, but not by THAT much



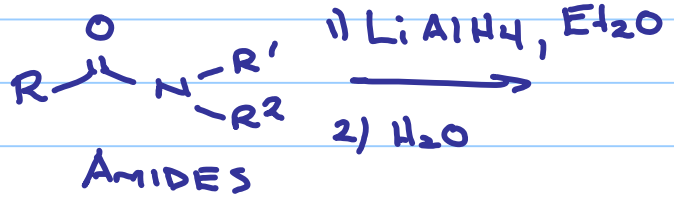
Reasoning

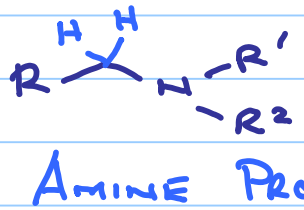


Constraint - Amine must be Cheap



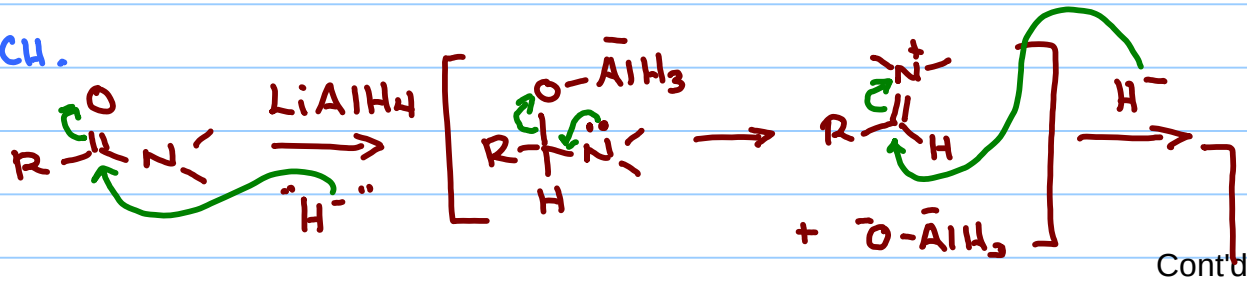
2) Reduction of Amides (Kart-1 20.6 B)





Amine Prod.
(not Alcohol!)

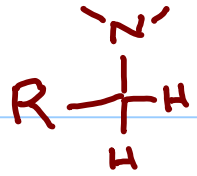
Mech.



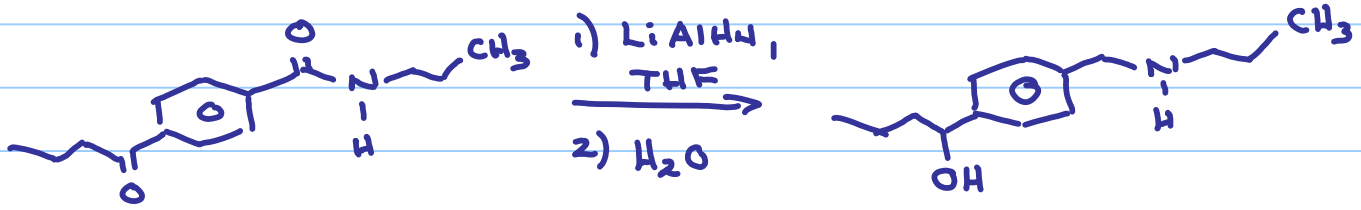
Cont'd

WON'T TEST THIS MECH.

Contd



NO POLYALKYLATION POSSIBLE



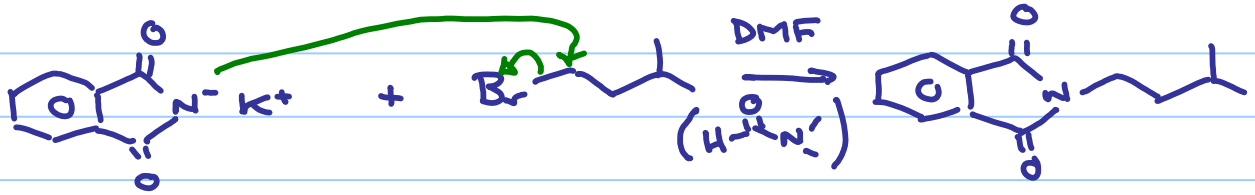
3) GABRIEL SYNTHESIS (KARTY 20.4)

- FOR 1° AMINES ($R-NH_2$) ONLY.

IMIDE

USE K^+ SALT BECAUSE IT'S MORE REACTIVE THAN Na^+ SALT

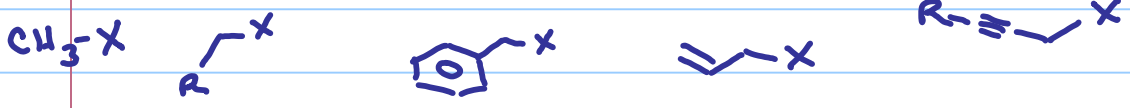
- ANION IS MODESTLY NUCLEOPHILIC



SHORTCOMING - NEED V. POLAR, APROTIC SOLVENT (DIMETHYLFORMAMIDE)

- ALKYL HALIDE MUST BE REACTIVE

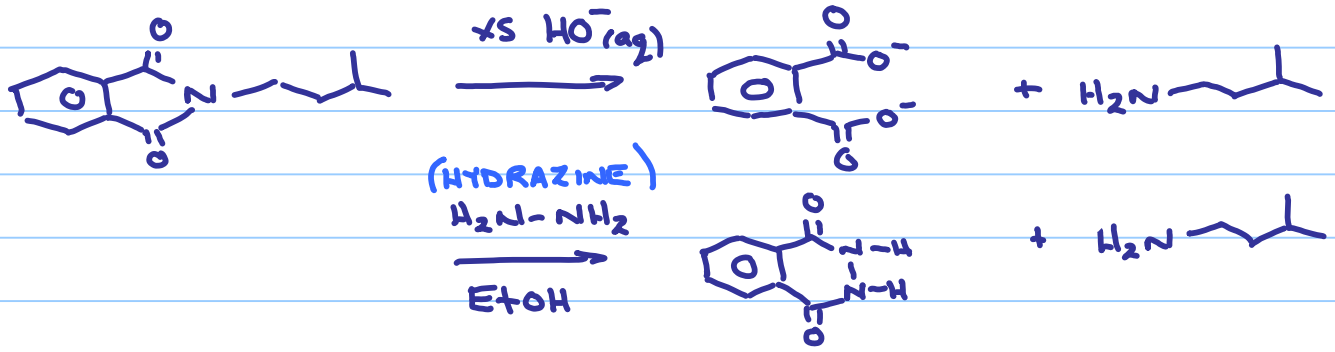
METHYL, 1°, BENZYLIC, ALLYLIC, PROPARGYLIC



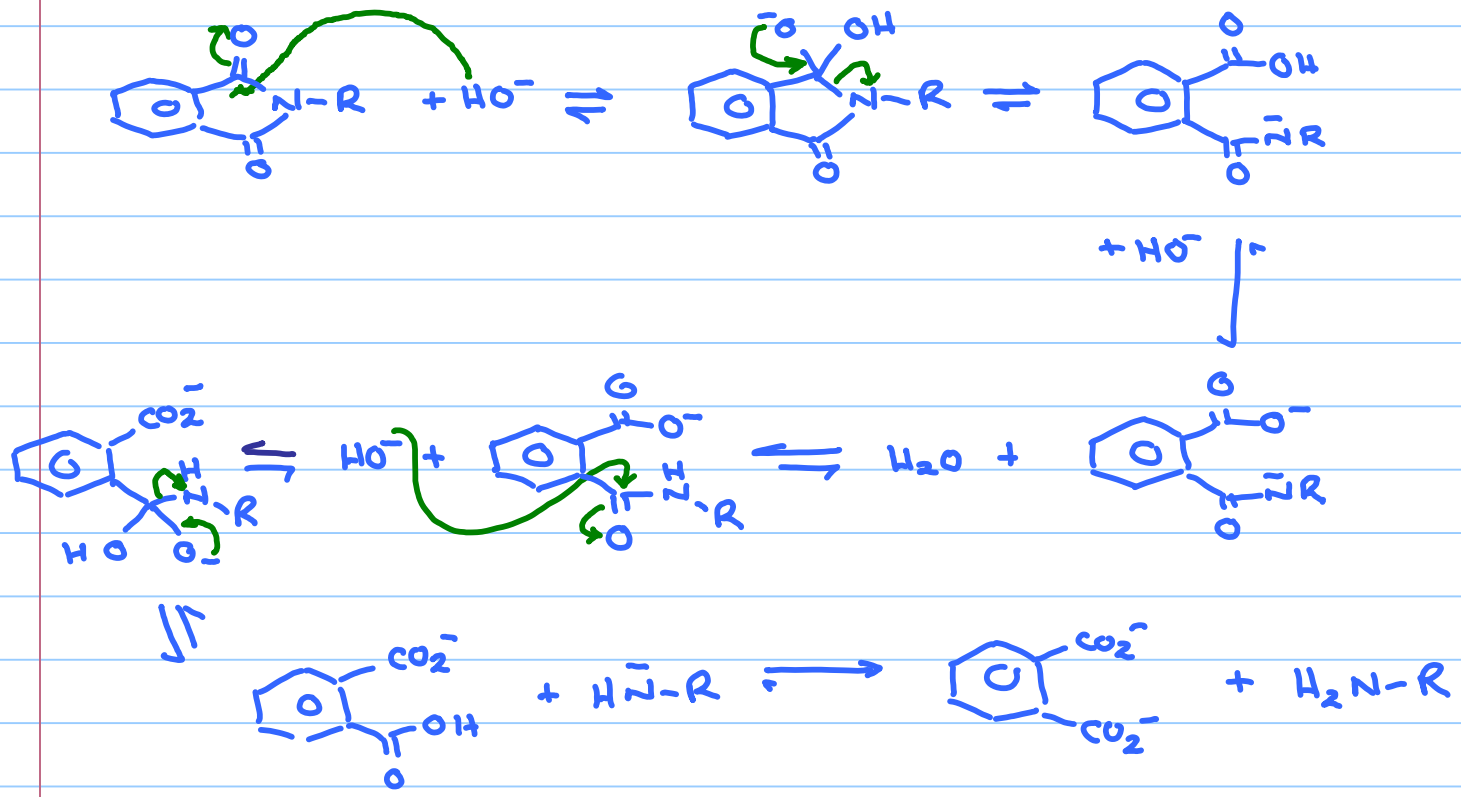
2° - NOPE

TOO SLOW

MUST LIBERATE AMINE – 'HYDROLYSIS' OF IMIDE



MECH. (USING HO⁻)



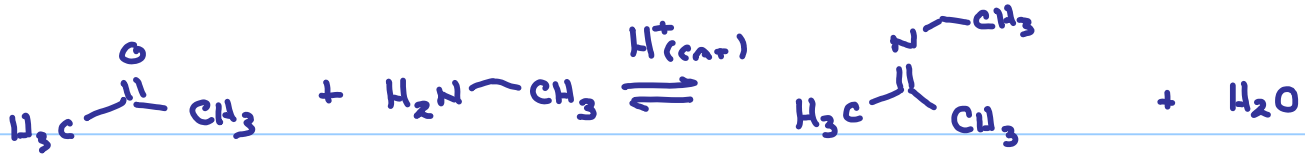
4) CYANIDE ION / NITRILES – SKIP THIS YEAR

5) REDUCTIVE AMINATION KARTY 18.2b & 17.3

2 RXNS COMBINED TOGETHER

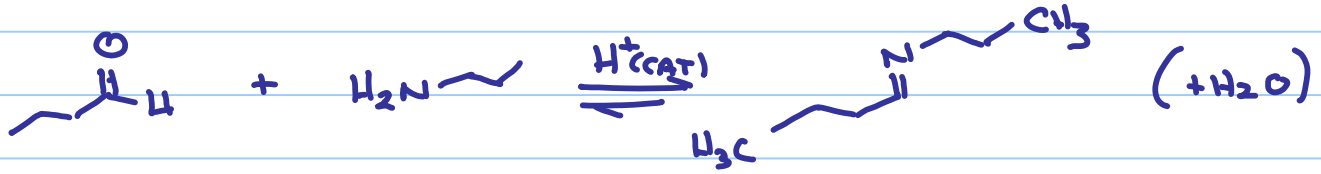
i) RXN OF AMMONIA / 1° AMINE W KETONE OR ALDEHYDE ⟶ IMINE

my mistake, I wrote "Amine" here in class
-it's "Imine"



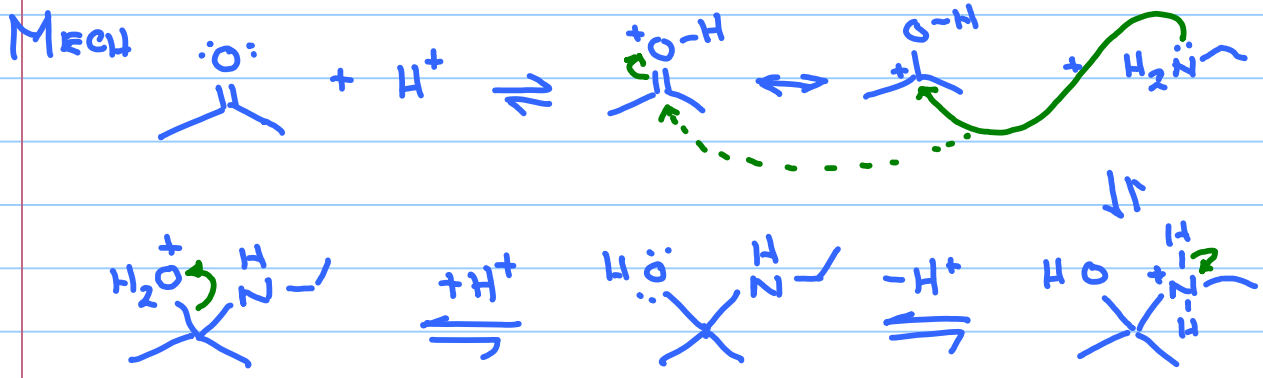
- RXN GOES AT ALL pH's ; FASTEST AT pH = 5

∴ H^+ RECOMMENDED, NOT MANDATORY

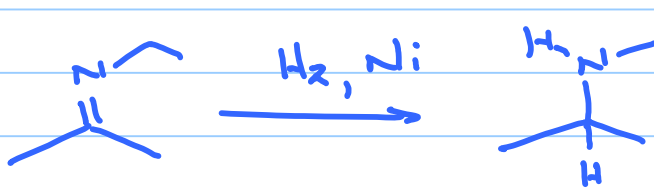


MOSTLY (E)- ISOMER, BUT (E)- + (Z)- INTERCONVERT READILY

MECH



2ND HALF



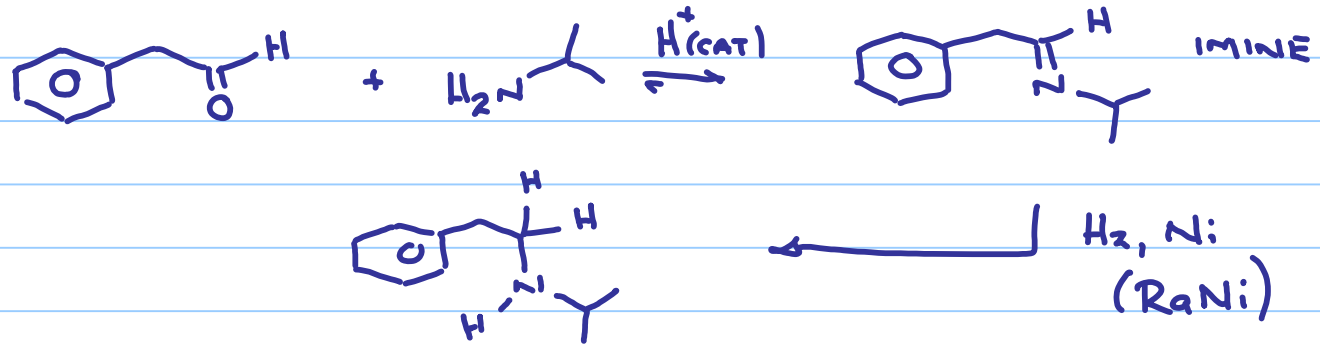
REDUCTION OF C=N

to be continued.....

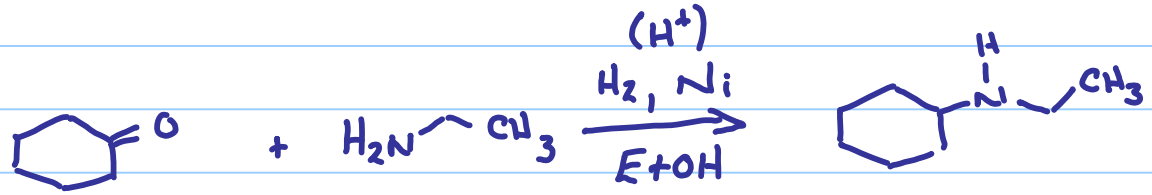
LECTURE 19

Note Title 3/22/2017

5) REDUCTIVE AMINATION
- 2 RXNS COMBINED

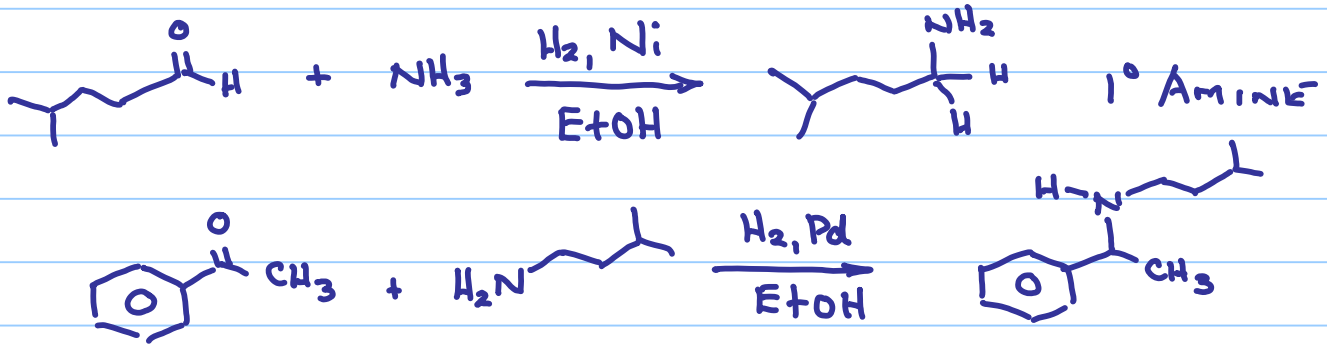


- GOOD NEWS - IMINES REDUCE BY CATALYTIC HYDROGENATION FASTER THAN ALDEHYDES/KETONES, SO WE CAN DO THESE TWO RXNS 'ALL AT ONCE'

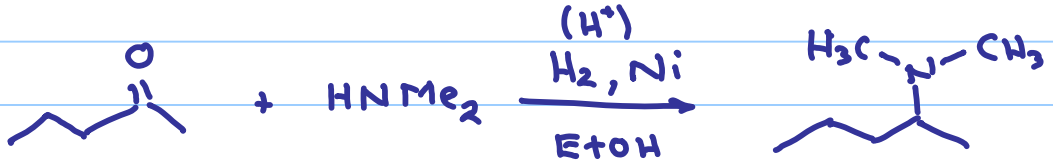


2° AMINE

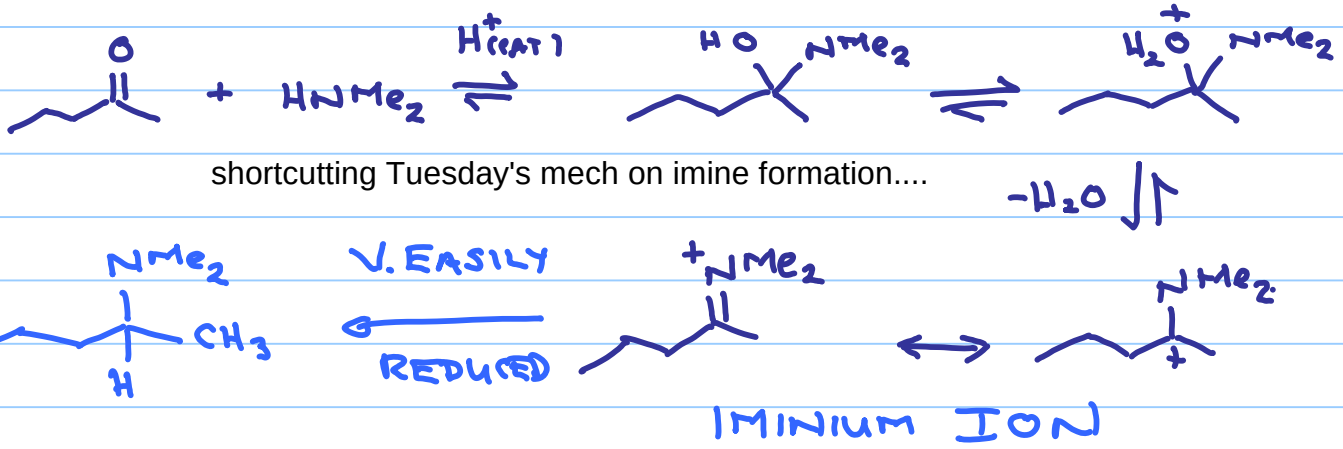
∴ VERY USEFUL & WIDE RANGING



RXN WORKS EVEN WITH 2° AMINES TO GIVE 3° AMINES



- REASON THIS WORKS BECAUSE - NO IMINE, BUT IMINIUM ION - THIS IS ALSO EASILY REDUCED



NOTE: $Na^+ \bar{B}H_3CN$ SODIUM CYANOBOROHYDRIDE

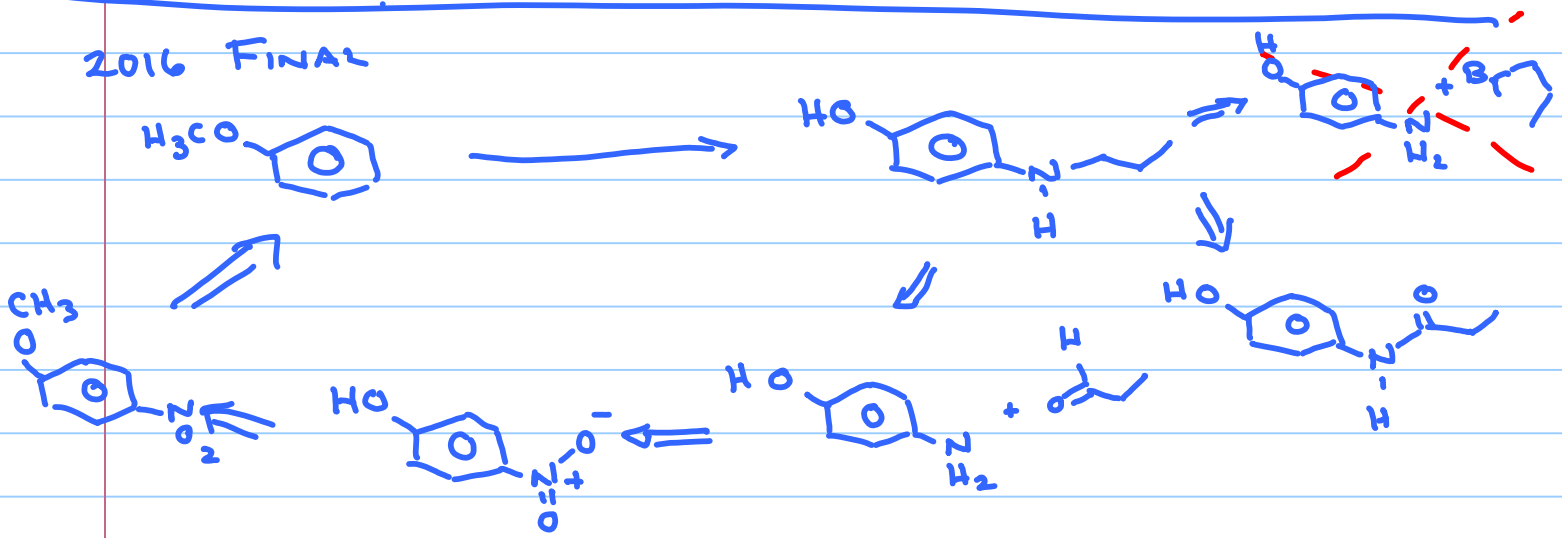
- WEAKER H^- DONOR THAN $NaBH_4$

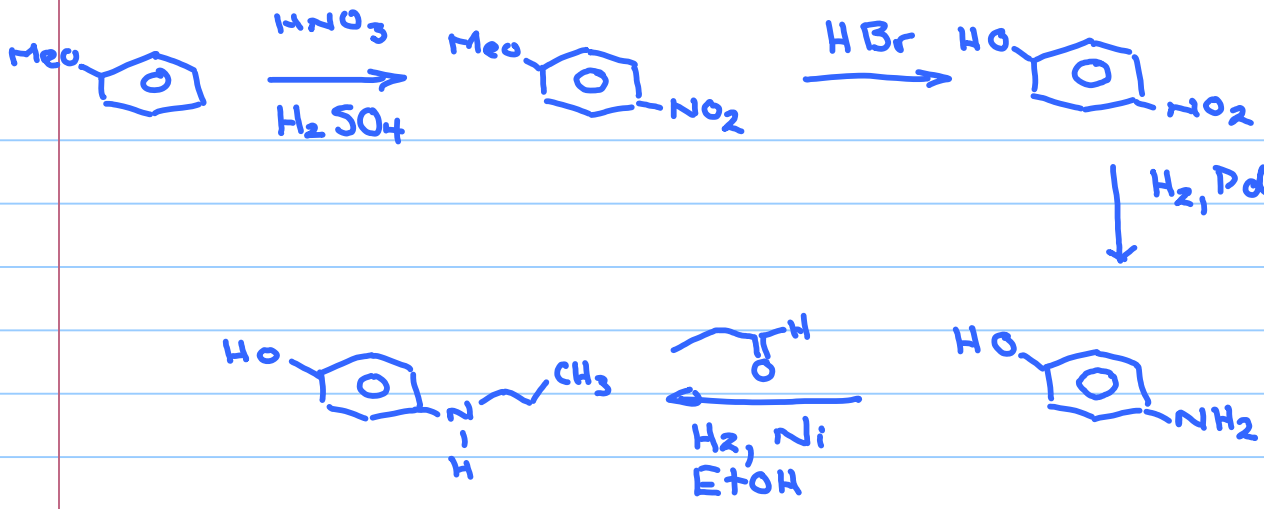
∴ SLUGGISH FOR ALDS/KETONES, BY V. REACTIVE FOR IMINIUM IONS

- SURVIVES SLIGHTLY ACIDIC CONDITIONS

∴ PERFECT FOR REDUCTNE AMINATIONS

2016 FINAL





Compound Characterization

CH 15, 16 Karty

- How do we know what an organic compound is?

Questions

1) What is the molecular formula?

   a) Elemental Analysis
      - Gives a C:H:N Ratio

   b) Mass Spectrometry (Spectroscopy)
      - Molar Mass / Molecular Weight

2) Where is everything Bonded?

   a) Infrared Spectroscopy (IR)
      - Looking for Major Functional Groups

   b) Nuclear Magnetic Resonance (NMR)

      - Local Environment of H atoms
      (can also be used for C, and other elements)

1a) ELEMENTAL ANALYSIS.

- BURN A CAREFULLY WEIGHED SAMPLE OF PURE MATERIAL

$C \rightarrow CO_2$ $\quad H \rightarrow H_2O$ $\quad N \rightarrow N_2$

- GET BACK A REPORT OF

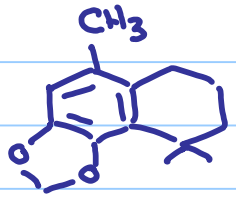
%C %H %N (%O)

DIVIDE $\frac{\%C}{12.011}$ $\frac{\%H}{1.008}$ $\frac{\%N}{14.007}$ $\frac{\%O}{15.999}$

- THEN, WE'LL TAKE EACH OF THESE + DIVIDE BY SMALLEST NUMBER OF THESE FOUR

$\Longrightarrow$ EMPERICAL FORMULA

- MOLECULAR FORMULA MAY BE EMPERICAL FORMULA, OR MAY 2X OR 3X OR 4X THE EMPERICAL FORMULA



C, $\frac{77.03\%}{12.011}$ $\quad$ H, $\frac{8.31\%}{1.007}$ $\quad$ O, $\frac{14.66\%}{15.999}$

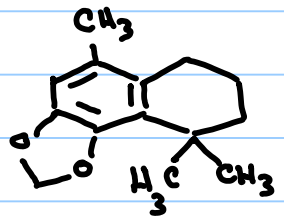
$= \frac{6.41}{.916}$ $\quad \frac{8.25}{.916}$ $\quad \frac{0.916}{.916}$

$= 7.00$ $\quad = 9.00$ $\quad = 1$

EMPERICAL FORMULA C_7H_9O

LECTURE 20

Note Title 3/28/2017



E.A. C, 77.03% H, 8.31% O, 14.66%

C_7 H_9 O_1

EMPERICAL FORMULA

- TO GET MOLECULAR FORMULA, TURN TO MASS SPECTROSCOPY

  - GIVES MOLAR MASS (MOLECULAR WEIGHT) OF YOUR COMPOUND
  - SIMPLEST EXPT. - BOMBARD SAMPLE W e^-'S
    - KNOCKS OUT AN e^- TO GIVE A RADICAL CATION

  - SEND IT THROUGH A MAGNETIC FIELD
    - HOW FAST IT BENDS TOWARD MAGNET DEPENDS UPON m/e

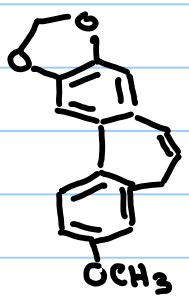
  IDEALLY m/e = MOLAR MASS

IN THE CURRENT CASE m/e (MOLECULAR ION) = 218

BUT $C_7 = 84$
$H_9 = 9$
$O = 16$
109

∴ MOLECULAR FORMULA IS $C_{14}H_{18}O_2$

- A SECOND CASE



C, 76.68 % ; H, 5.30 % ; O, 18.02 %

	$\frac{76.68\ \%}{12.011}$	$\frac{5.30\ \%}{1.007}$	$\frac{18.02\ \%}{15.999}$
	$= \frac{6.384}{1.126}$	$= \frac{5.26}{1.126}$	$= \frac{1.126}{1.126}$
	= 5.67	= 4.67	= 1 NO WAY
×2	11.34	9.34	2
×3	17.01	14.01	3 ⇐

EMPERICAL FORMULA = $C_{17} H_{14} O_3$

MASS SPECTRUM $m/e = 266$

FITS ∴ MOLECULAR FORMULA IS $C_{17} H_{14} O_3$

ALMOST NO STRUCTURAL INFO, EXCEPT

INDEX OF HYDROGEN DEFICIENCY (IHD)

$$IHD = \frac{2c + 2 - h - x + n}{2}$$

c = # OF C ATOMS h = # OF H ATOMS

x = # OF HALOGEN ATOMS n = # OF N ATOMS

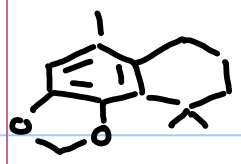
FOR $C_{17} H_{14} O_3$ $IHD = \frac{34 + 2 - 14}{2} = \frac{22}{2} = 11$

C=O OR C=N OR C=C GIVES 1

RING GIVES 1

C≡C OR C≡N GIVE 2

SUM OF ALL THESE = 11



IHD = 6

$C_{14}H_{18}O_2$

$$IHD = \frac{28 + 2 - 18}{2} = \frac{12}{2} = 6$$

NOW TO SPECTROSCOPIC METHODS.

1) NMR (NUCLEAR MAGNETIC RESONANCE) SPECTROSCOPY
   - ESPECIALLY ^1H NMR
2) IR (INFRARED SPECTROSCOPY)

NMR.

- MOST NUCLEI HAVE NUCLEAR SPIN
- SIMPLEST OF ALL IS H ATOM W 1 PROTON, NO DEUTERON
  (^1H (PROTON) NMR SPECTROSCOPY)

this is the basis for MRI, magnetic resonance imaging.....

- IN A MAGNETIC FIELD $\vec{B}$
  - THE PROTON CAN ALIGN WITH FIELD (LOWER ENERGY)
  - PROTON CAN ALIGN AGAINST FIELD (HIGHER ENERGY)

- IRRADIATE SAMPLE WITH RADIOFREQUENCY E, THE NUCLEUS WILL ABSORB THAT ENERGY GO FROM LOWER TO HIGHER E SPIN STATE

$\vec{B}$	^1H FREQUENCY
1.41 T	60 MHz
7.05 T	300 MHz
11.7 T	500 MHz

$= 2 \times 10^{-4}$ kJ/mol

weakest bond = 140 kJ/mol, so NMR spectrscopy is non-destructive

- NOT EVERY H ATOM UNDERGOES RESONANCE AT EXACTLY 300 MHz

RANGE OF ≈ 3000 Hz

$$\therefore \frac{3000\ Hz}{300 \times 10^{6}\ Hz} = 10 \times 10^{-6} \quad \text{OR} \quad 10\ ppm$$

- FOR ^1H NMR SPECTROSCOPY, 95% OF PROTONS UNDERGO RESONANCE IN THIS 10 ppm RANGE

- A STANDARD HAS BEEN CHOSEN TO BE CALLED ZERO

TMS = $Si(CH_3)_4$ = 0 ppm

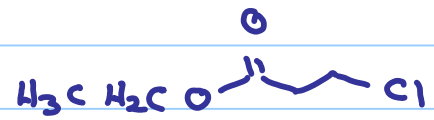
- EVERYTHING ELSE IS SAID TO HAVE A CHEMICAL SHIFT (δ) RELATIVE TO TMS

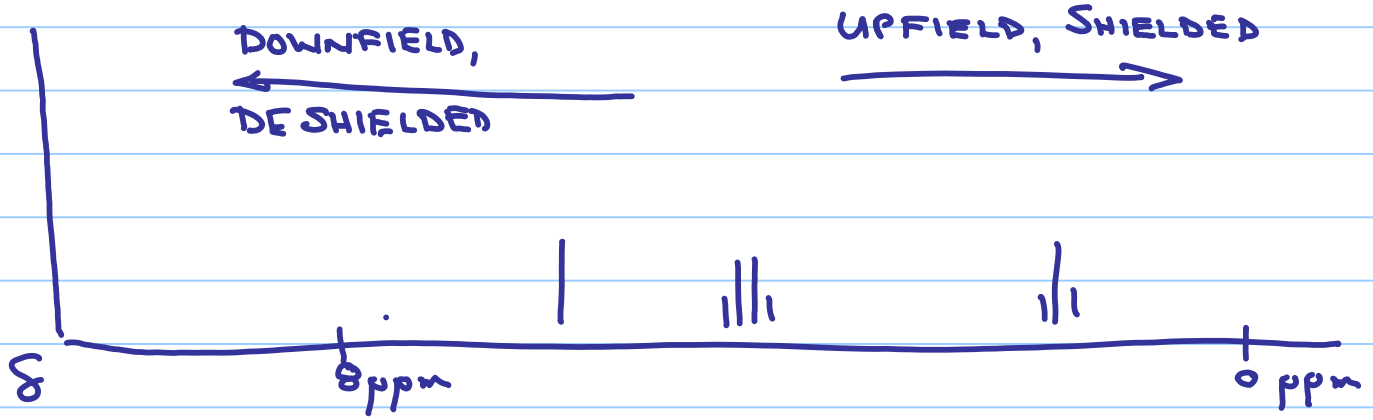
85% OF H ATOMS HAVE A δ = 0.5 - 8.3 ppm

13% δ = 8.3 - 12 ppm

2% δ < 0 ppm

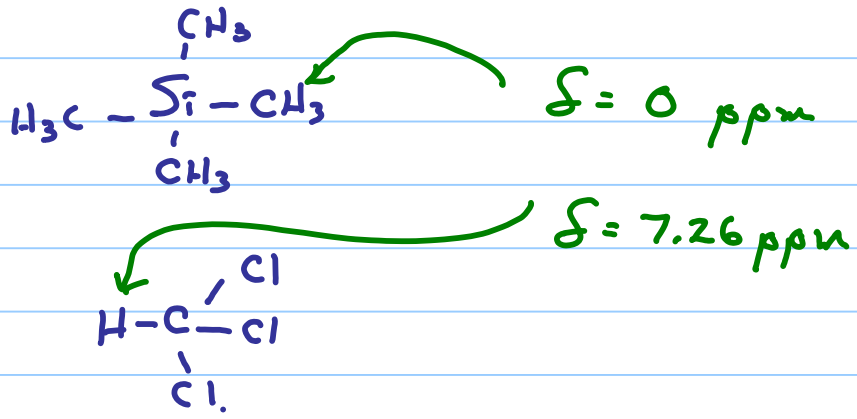
CALLED CHEMICAL SHIFTS

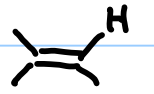
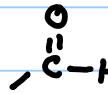




- H ATOMS NOT NEAR EN GROUPS HAVE A SIGNIFICANT AMOUNT OF e^- DENSITY NEAR ^1H NUCLEUS - "SHIELDS" H ATOM FROM THE APPLIED $\mathcal{H}$ $\therefore$ LOWER δ

- H ATOMS NEAR EN ATOMS, NOT MUCH e^- DENSITY NEAR H ATOM TO SHIELD IT FROM THE APPLIED $\mathcal{H}$ $\therefore$ DESHIELDED, HIGHER δ



GENERAL TRENDS		δ (ppm)
SIMPLE ALKANES	$CH_3CH_2CH_2$-	1
- ALKYLS ONE ATOM FROM HETEROATOM - ALKYLS NEXT	$HO-CH_2-CH_3$	1-2
- ALKYLS NEXT TO A CARBONYL - ALKYLS NEXT TO AN AMINE	$-C(=O)-CH_3$ $-N-CH_3$	2-3
- ALKYLS NEXT TO 'O' ATOM	$O-CH_2-$	3-4.3
- ALKENE H'S		5's + 6's
- AROMATIC S		6.8 - 8.3
- ALDEHYDES		9-10

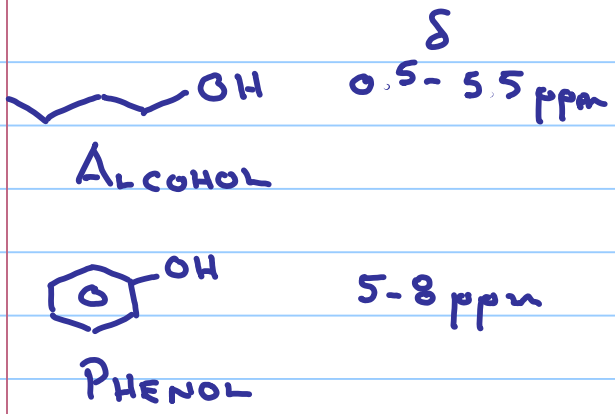
Lecture 21

Note Title 3/30/2017

NMR spectroscopy, cont'd)

OH's, NH's

- Involved in H Bonding
  ∴ Exchanging between O's (or N's)
∴ δ Concentration, Temperature, Solvent Dependent
- Wide Range of Chemical Shift (δ) Possible



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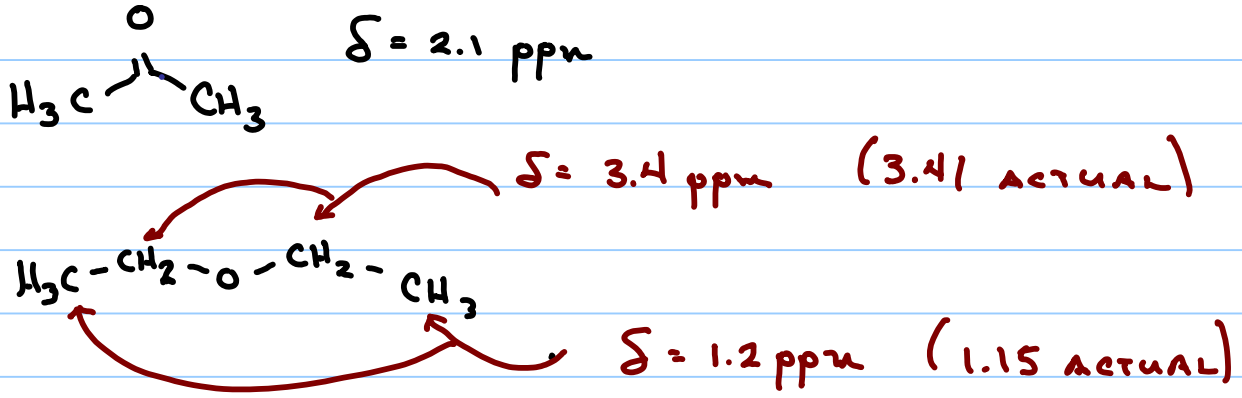
some examples

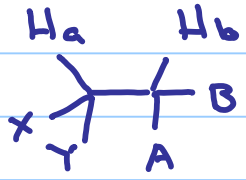


Integrals - in ^1H NMR Spectra, the Area underneath each Resonance is Proportional to the # of H atoms it Represents

For Diethyl Ether δ 3.4 ppm, A = 4

δ 1.2 ppm, A = 6

That Splitting of Peaks.
Spin - Spin Splitting



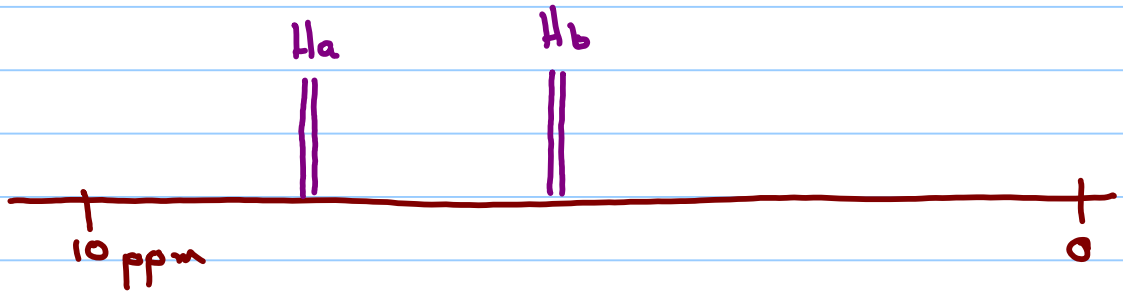
For Ha at Resonance, Two Possibilities

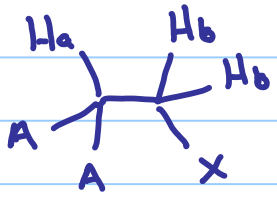
i) where Hb is Algned with ℋ

ii) where Hb is Against ℋ

∴ Ha appears a 2 Closely Spaced Lines

Doublet (d)



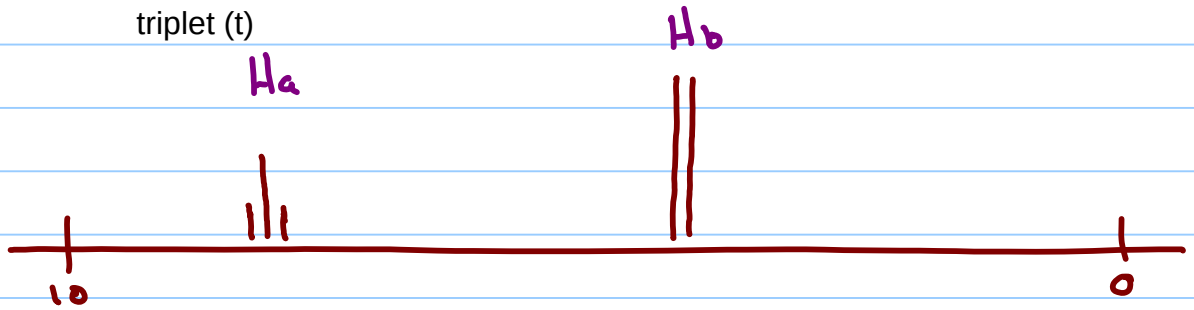


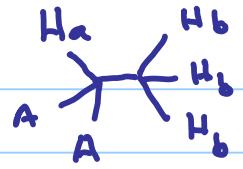
For Ha 3 Possibilities

i) Hb's Both Against ℋ

ii) One Hb with / One Hb Against } ℋ (Twice as Likely)

iii) Both Hb's With ℋ





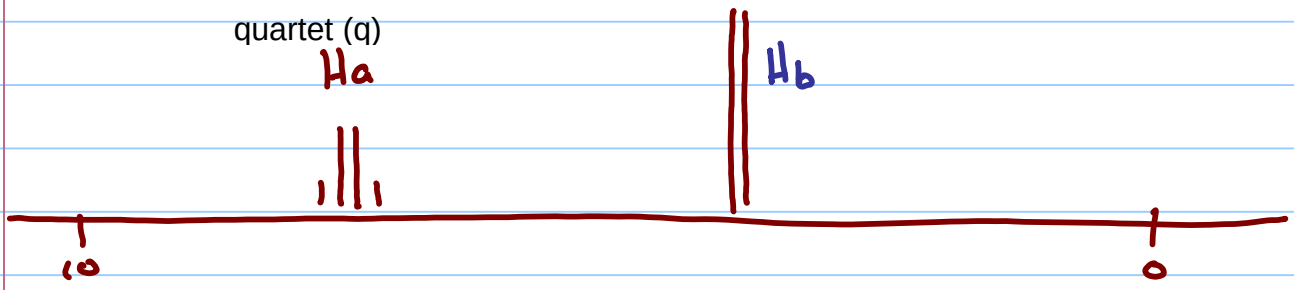
4 POSSIBILITIES FOR Ha

i) ALL 3 Hb's WITH ↑↑↑

ii) 2 Hb's WITH ↑, 1 AGAINST ↑↑↓

iii) 2 Hb's AGAINST ↓, 1 WITH ↑↓↓

iv) ALL 3 Hb's AGAINST ↓↓↓



CALLED THE "n+1 RULE"

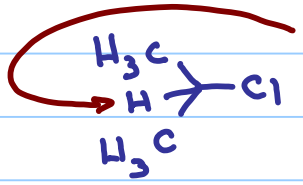
OF H'S NEXT DOOR + 1 = MULTIPLICITY.

INTENSITIES OF EACH LINE are given by...

PASCALS TRIANGLE

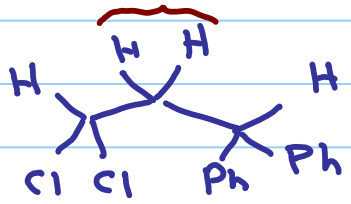
	# NEXT DOOR
1	
1 1	1
1 2 1	2
1 3 3 1	3
1 4 6 4 1	4

- SOME EXAMPLES



NEXT TO 6 CHEMICALLY IDENTICAL H'S

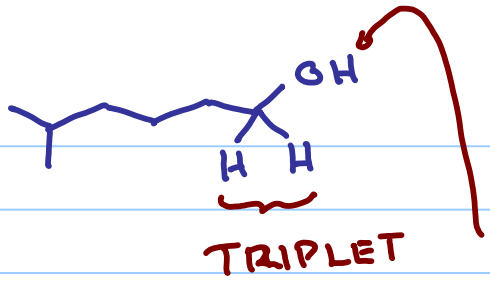
∴ SEPTET



NEXT TO 1 CHEMICALLY DIFFERENT H ON EACH SIDE

DOUBLET OF DOUBLETS

(NOT A 'TRIPLET', ALTHOUGH IT MIGHT LOOK LIKE ONE)



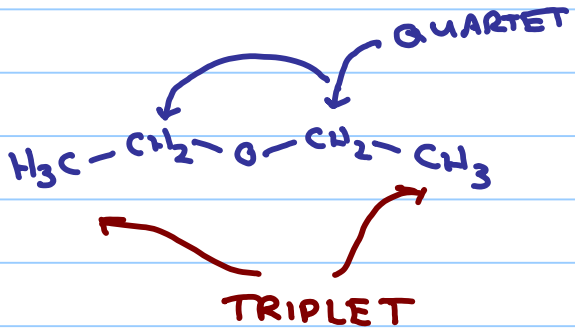
OH'S & NH'S DON'T PLAY IN SPLITTING, DUE TO THEIR RAPID EXCHANGE

TRIPLET

due to CH2 on other side

SINGLET (MAYBE A BIT BROAD)

BACK TO



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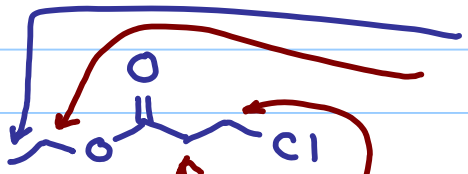
so let's do a complete prediction for ethyl 3-chloropropanoate



$\delta = 1.3$, t, A = 3

$\delta = 4.1$, q, A = 2

$\delta = 2.2 + (0.6) = 2.8$, t, A = 2

$\delta = 3.4 + (0.5) = 3.9$, t, A = 2

Note: If you see a quartet, A = 2, at ca. 4.2 ppm and a triplet, A = 3 at ca. 1.3 ppm, it's almost always a giveaway for an ethyl ester.

Lecture 22

Note Title 4/4/2017

Final Exam Fri. Apr. 21 Noon - 3 PM
Ambassador Auditorium

Get an 'IR' Table

IR (Infrared) Spectroscopy

- Based on the idea that a Bond is Like a Spring
- If You Hit the Molecule with the Proper ν of Radiation, that Bond will Stretch, or Bend, or Twist, or Rock
- Those ν's are V. Characteristic of the Functional Group

- Energy Concerned 8-40 kJ/mol (Below Visible Light)
- Units are $1/\lambda_{(cm)}$ (cm^{-1}) this is a frequency, despite the odd units
  - Called Wavenumbers $\bar{\nu}$

Range 4000 - 600 cm^{-1}

$\bar{\nu}$ Depends on

1) Process - Stretch, Bend, Twist?

2) Strength of the Bond

C≡C	C=C	C-C
2150 cm^{-1}	1650 cm^{-1}	1200 cm^{-1}

3) Size of the Groups on Each End of the Bond (Reduced Mass)

C – H	C – O	C – Br
3000 cm^{-1}	1100 cm^{-1}	550 cm^{-1}

Spectrum Artificially Divided into 2 Parts

1) Characteristic Functional Group Range
   4000 – 1500 cm^{-1}

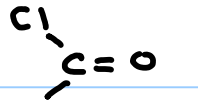
2) Fingerprint Region
   1500 – 600 cm^{-1}

Bonds that are Polar Show up much more Intensely.

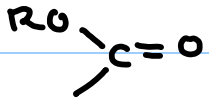
Characteristic Groups.

O–H	3300 cm^{-1}	broad	Alcohol
	3000 cm^{-1}	V.V. broad	Acid
N–H	3300 cm^{-1}	Less intense than Alcohol	Amines
C–H	~ 3000 cm^{-1}	< 3000 cm^{-1}	sp^3 C–H
		> 3000 cm^{-1}	sp^2
		3300 cm^{-1}	sp
C≡N	2250 cm^{-1}	Medium to Strong	
C≡C	2150 cm^{-1}	Weak to Medium	

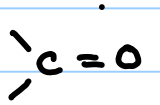
C=O



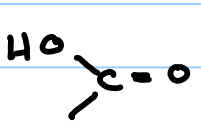
1800 cm^{-1}



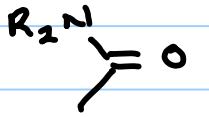
1740 cm^{-1}



1710 cm^{-1}



1700 cm^{-1}



1660 cm^{-1}

IF CONJUGATED TO A C=C, C≡C, OR 

↓ DROPS BY 30 cm^{-1}

C=C

C=C ALKENE 1600 - 1650 cm^{-1}

WEAKER THAN C=O

 BENZENES 2 BANDS

1600 & 1500 cm^{-1}

END

FINAL 2016 SPEC Q

m/e 116

C, 62.04% ÷ 12.011 = 5.163 / 1.722 = 3

H, 10.41% ÷ 1.008 = 10.33 / 1.722 = 6

O, 27.55 ÷ 15.999 = 1.722 / 1.722 = 1

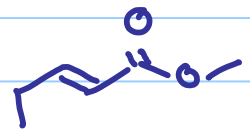
EMPERICAL FORMULA IS C_3H_6O

C 36
H 6
O 16
} : 58

BUT MASS SPEC m/e IS 116

∴ MOLECULAR FORMULA IS $C_6H_{12}O_2$

$$IHD = \frac{2(6)+2-12}{2} = 1$$

 IS OUT OF THE RUNNING

GO TO IR SPECTRUM

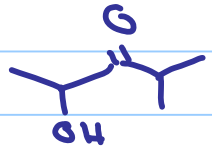
3390 cm^{-1} O-H STRETCH ALCOHOL

2969 cm^{-1} C-H STRETCH sp^3 C-H

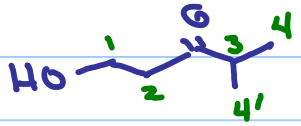
1715 cm^{-1} C=O STRETCH, MOST LIKELY OF KETONE

 OUT, BECAUSE NO C=O
(ALSO NOT ∃ C=C)

 NEEDS $\nu_{C=O}$ 1735-1740 cm^{-1}

LEAVES US  & 

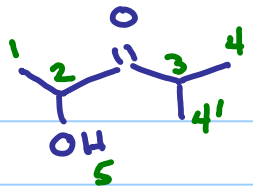
NOW TO NMR

TRY 

① PREDICT $\delta = 3.4 + (0.4) = 3.8$, A=2, t — NO MATCH

② $\delta = 2.3 + (0.3) = 2.6$, A=2, t — NO MATCH

FAILS!



PREDICT

① δ = 1.1 + (0.4) = 1.5, A=3, d — MATCH

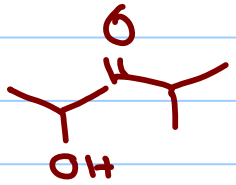
② δ = 2.6 + (2.2) = 4.8, A=1, q — ACCEPTABLE

③ δ = 2.6, , A=1, septet — GOOD MATCH

(4,4') δ = 1.1 ppm — A=6, d — GOOD MATCH

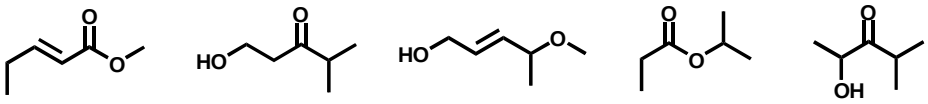
⑤ δ = 0.5-5.5 ppm, A=1, s — GOOD MATCH

THIS IS IT!

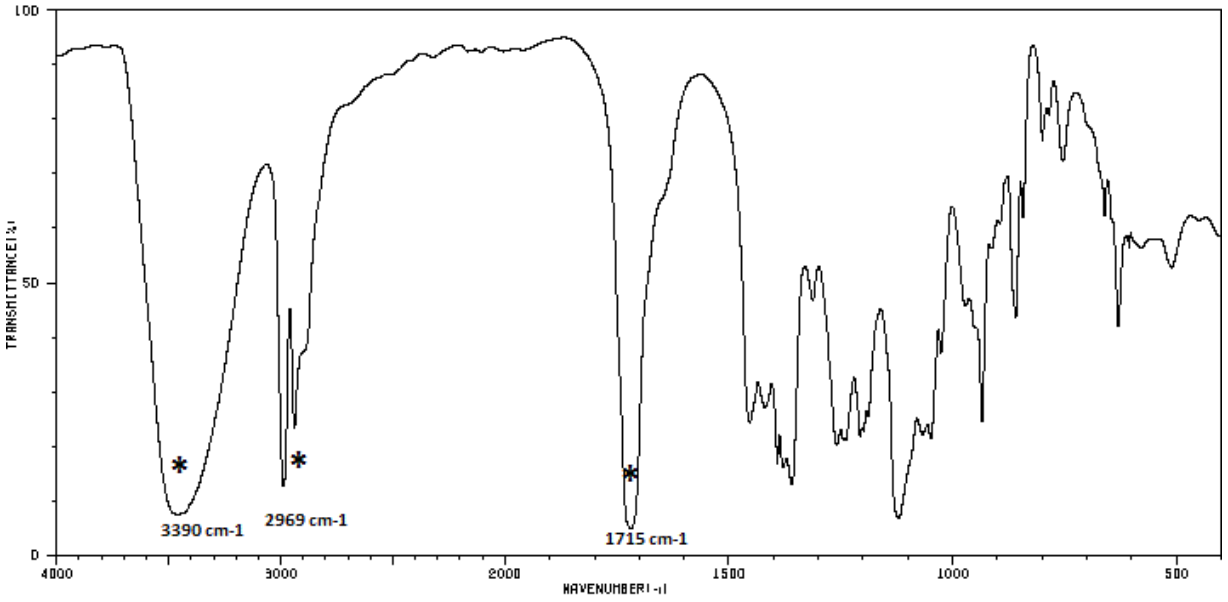


2016 Final Exam Spec Question

7. The following compound has been analyzed, revealing a composition C, 62.04%; H, 10.41%; O, 27.55%. The mass spectrum gives a highest m/e of 116. The IR (infrared) and ^{1}H NMR spectra are also included below. Which of the following structures is the most reasonable candidate for the compound in question, and why? Assign the ^{1}H NMR spectrum, showing the comparison of your calculated chemical shifts with the observed ones. Your answer should include the assignment of the most important features (i.e., the starred ones) of the IR spectrum. (**15 marks**)



IR



^{1}H NMR