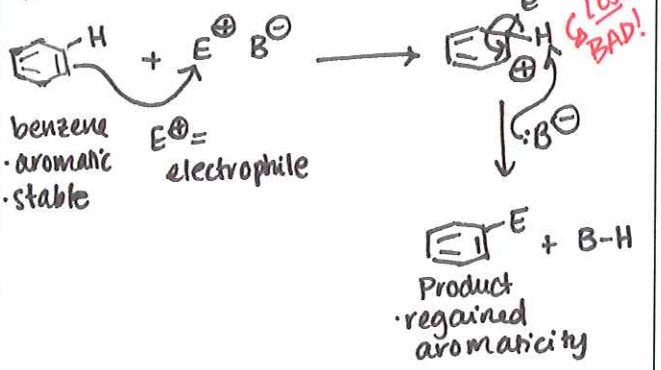
① WEEK 3-4: Electrophilic Aromatic Substitution

General Rxn:



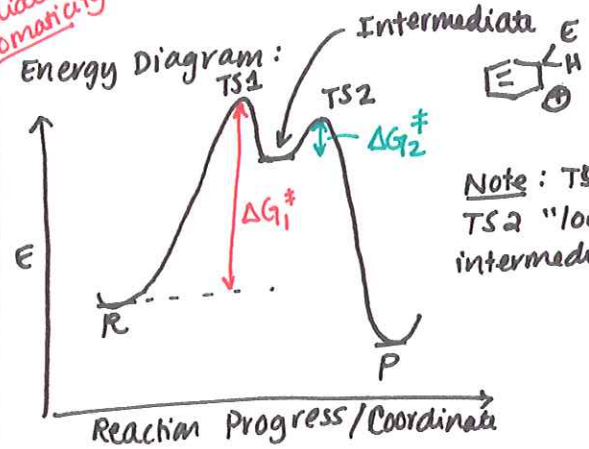
benzene
- aromatic
- stable

$E^{\oplus}$ = electrophile

Product
- regained aromaticity

②

Energy Diagram:

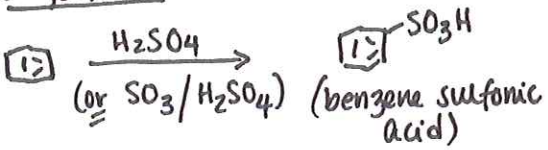


Note: TS1 & TS2 "look like" intermediate.

Conclusions:
(a) Losing aromaticity is hard; $\Delta G_1^{\ddagger}$ is large.
(b) Aromaticity is easily regained. $\Delta G_2^{\ddagger} \ll \Delta G_1^{\ddagger}$

③ Specific Electrophilic Aromatic Substns:

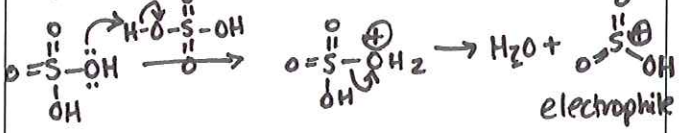
Sulfonation



(benzene sulfonic acid)

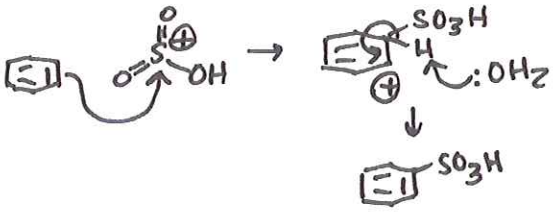
Mechanism:

Step 1: Generate "hot" electrophile:

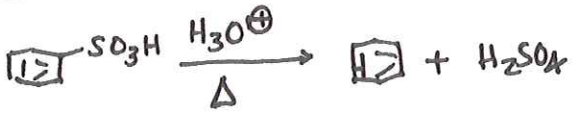


④

Step 2: React w/ benzene:

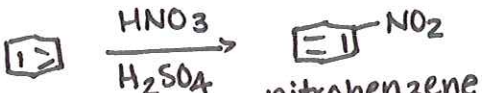


Note: Sulfonation is reversible !!



⑤

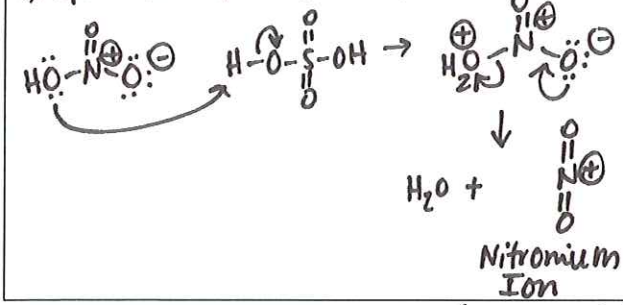
Nitration (Recall 1st Lab)



nitrobenzene

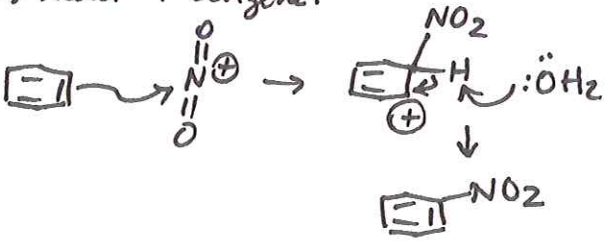
Mechanism:

1) Generate "hot" electrophile:

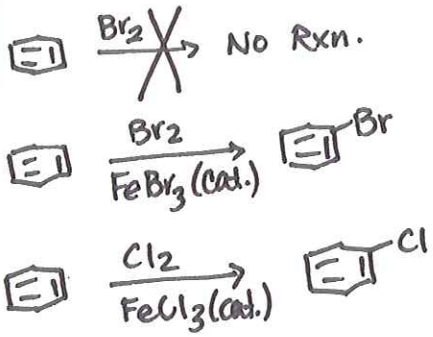


⑥

2) React w/ benzene:



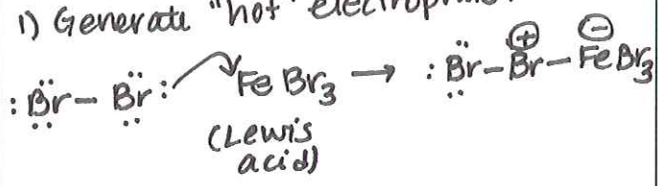
⑦ Lewis Acid-Catalyzed Halogenation



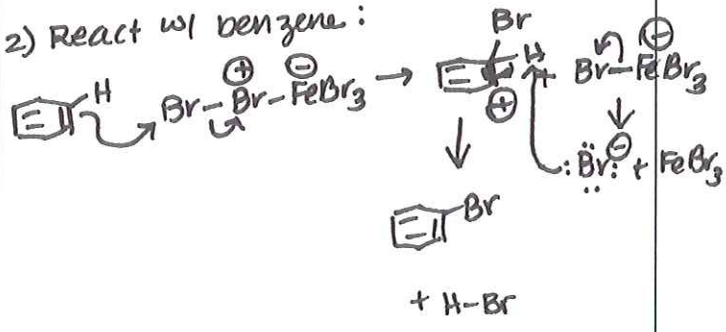
⑧

Mechanism:

1) Generate "hot" electrophile:

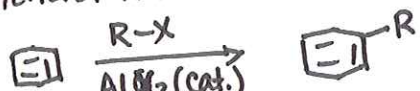


2) React w/ benzene:



⑨ Friedel-Crafts Alkylation

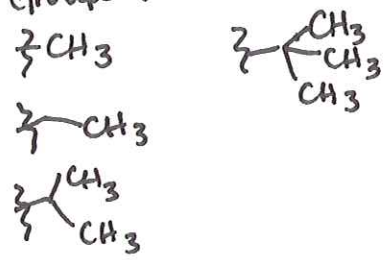
General Rxn:



where X = Cl, Br

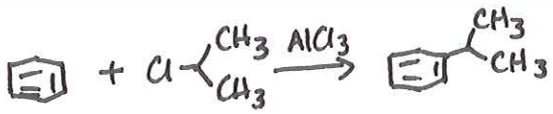
Alkyl Groups that work well:

R=



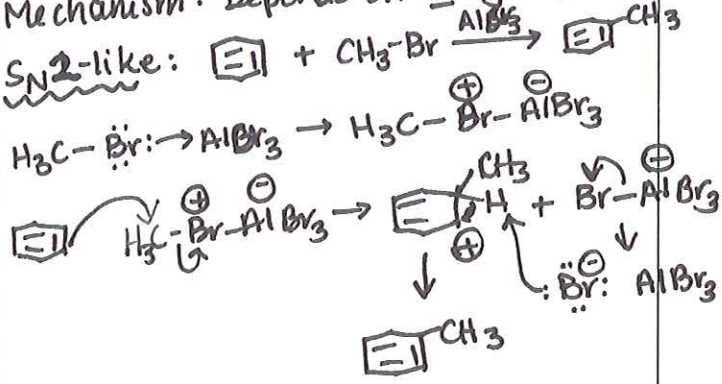
⑩

ex:



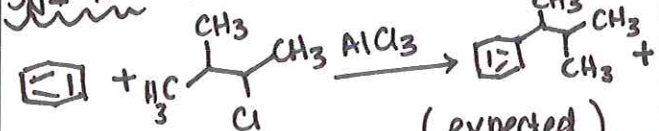
Mechanism: Depends on R group.

S_N2-like:



⑪

S_N1-like: WATCH FOR REARRANGEMENTS!!



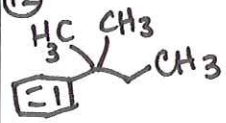
(not on our Good Alkyl Groups list)

(expected product)

30%

What happened?!?

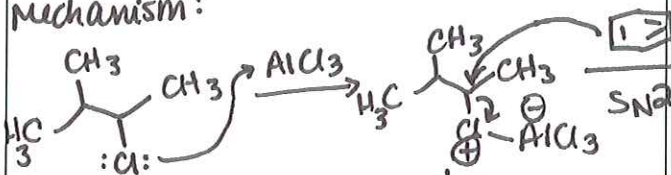
⑫

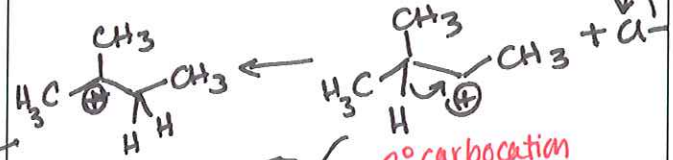


70%

(13)

Mechanism:





3° carbocation intermediate

2° carbocation intermediate

70% (3° carbocation = more stable)

30%

(14)

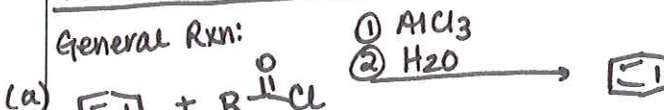
Maybe possible, but not favored! (Too sterically crowded)

(Benzene reacts w/ BOTH intermediates)

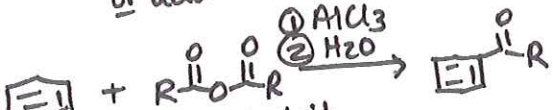
(15)

Friedel-Crafts Acylation

General Rxn:



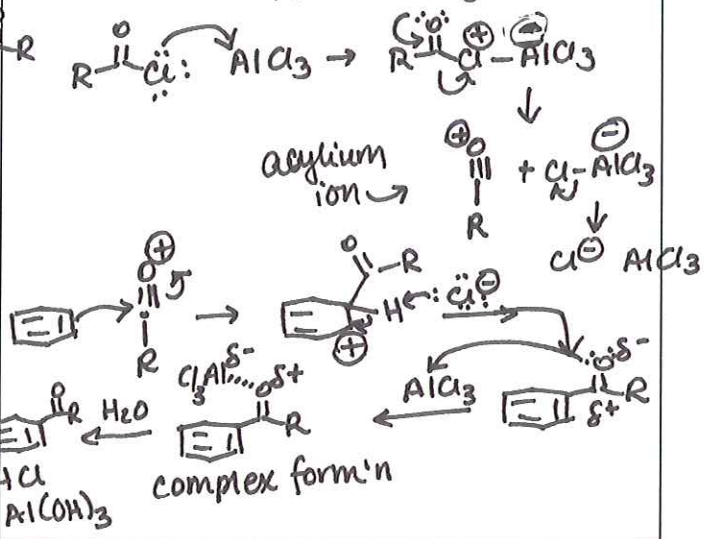
(a) acyl chloride or acid chloride



(b) acyl anhydride

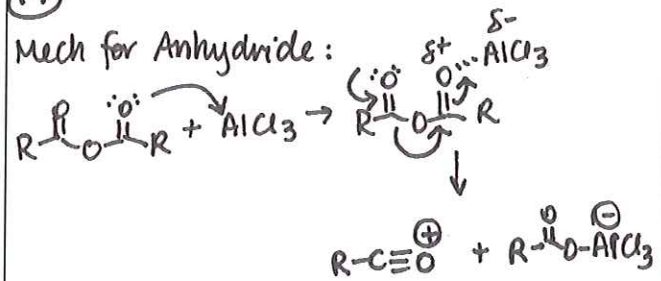
$AlCl_3$ ≠ catalyst.
(Must be used in stoichiometric amts)

(16) Mechanism: (Note: Acylation NOT prone to rearrangements)

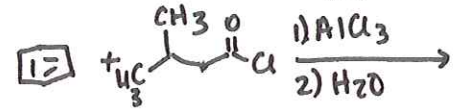


(17)

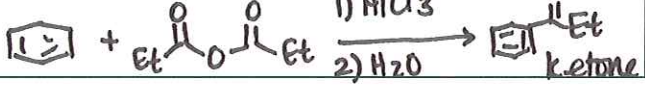
Mech for Anhydride:



ex:



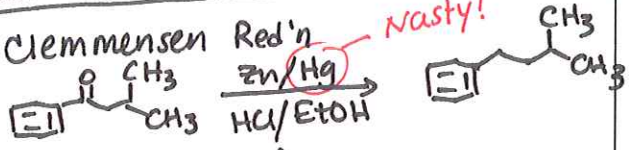
ex:



(18)

Aside: Reduction of Ketones: 2 Methods

① Clemmensen Red'n



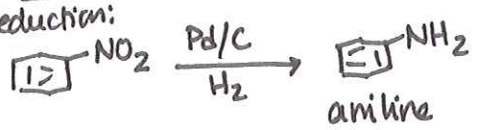
Nasty!

② Wolff-Kishner Red'n

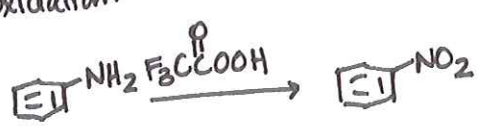
This means you can obtain alkyl substitutions not possible by F-C alkylation by doing F-C acylation + reduction (2 steps).

(19) **Interconversion of Nitrobenzene & Aniline**

Reduction:

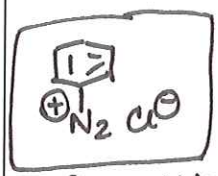


Oxidation:



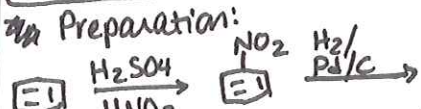
(20) **Benzene diazonium chloride**

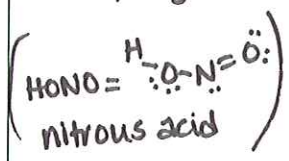
- key intermediate to substituted benzenes.



mechanism on p. 648.

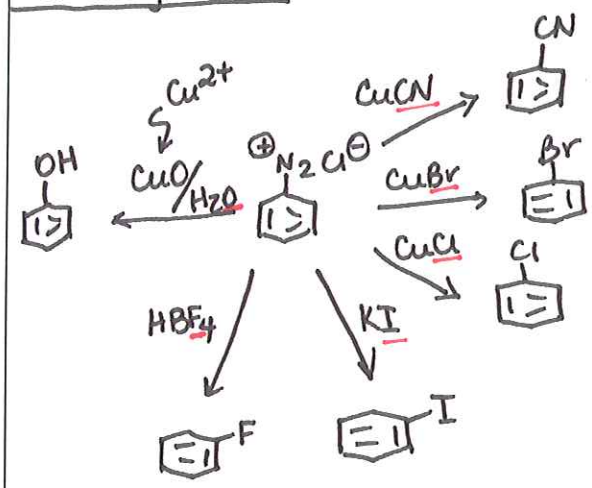
Preparation:





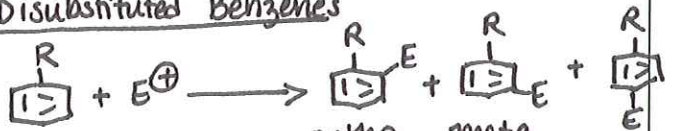
EXPLOSIVE WHEN DRY!!

(21) **Sandmeyer Rxns:**



Mechanisms not fully known.

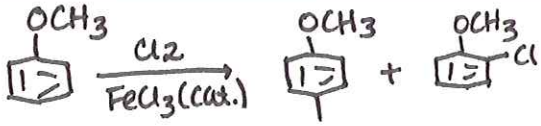
(22) **Disubstituted Benzenes**



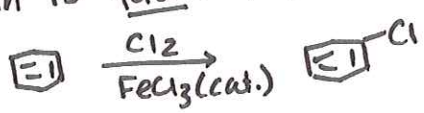
R influences:

1) Substitution Pattern
   o/p vs. m
2) Rate of Rxn (compared to benzene)
   Slower ⇒ R = Deactivating
   Faster ⇒ R = Activating

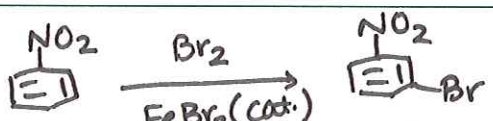
(23) ex:



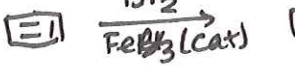
- No meta-substitution.
- Rxn is faster than



(24) ex:



Rxn is very slow compared to



SEE HANDOUT

In general: o/p-directors are faster compared to benzene (except halides).
m-directors are slower.