Substituent Effects on Reactivity and Orientation in EAS January 31, 2020

- Friedel Crafts & the Clemmensen and Wolff-Kishner reductions.
- Substituent effects on reactivity in EAS reactions.
- Substituent effects on orientation in EAS reactions.
- Why are NH_2 and OH strong activators & o,p directors?
- Why are halogens weakly deactivating and o,p directors?
- Synthetic applications.

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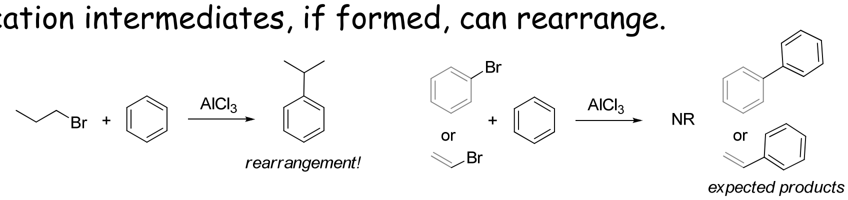
O'Leary office hours: T/Th 9:00-10:00 am, SN 208.

O'Leary's evening review session: Wednesdays 7:00 PM, SN Aud. **Course website**: http://pages.pomona.edu/~djo04747/110/

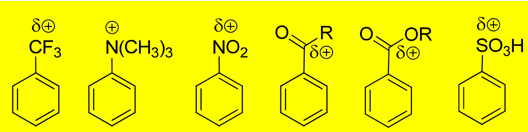
Suggested Problems for Exam 1. 10e/11e/Chapter 14: 18, 24, 26, 27, 28, 31, 33, 35. 10e/Chapter 15: 24, 25, 27, 28, 34abc, 43, 51. 11e/Chapter 15: 22, 23, 25, 26, 32abc, 41, 49.

Friedel-Crafts: Limitations

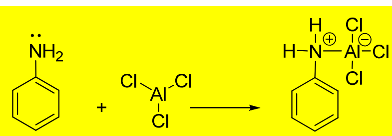
1. Carbocation intermediates, if formed, can rearrange.



2. Electron-withdrawing groups (EWG) shut down F-C reactions.

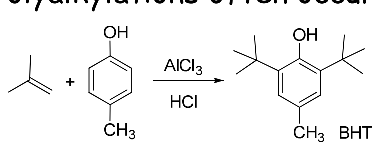


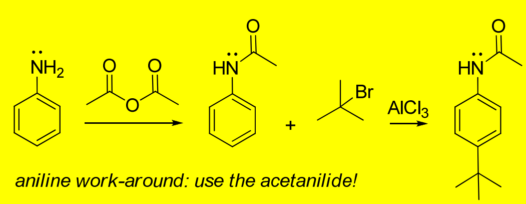
these substituents deactivate the ring and make F-C difficult



aniline derivatives fail for a related reason

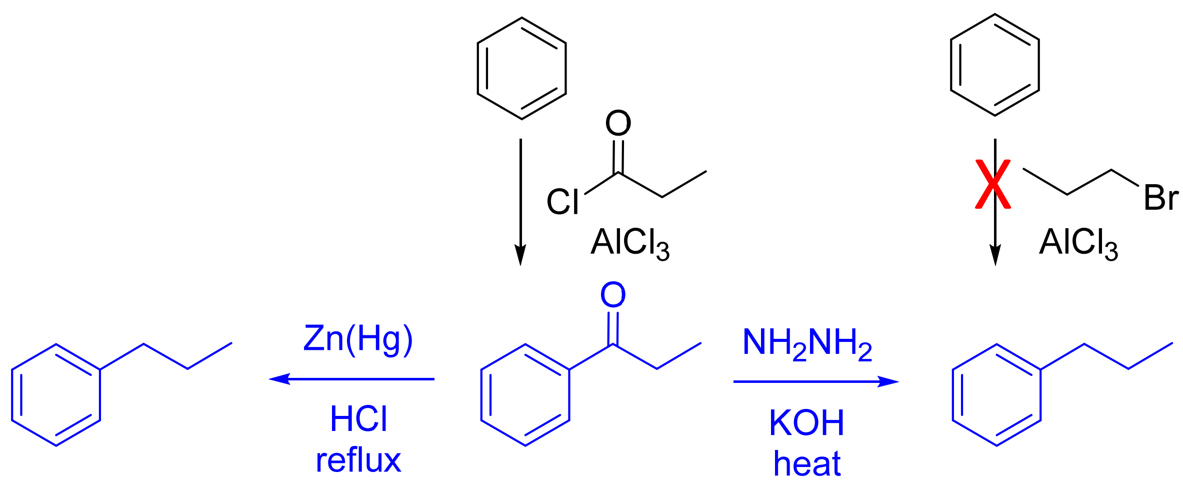
3. Polyalkylations often occur.





aniline work-around: use the acetanilide!

Clemmensen & Wolff-Kishner Reductions: A Typical Application



•Reduction mechanisms fall beyond the scope of this course.

EAS Free-Energy Diagram

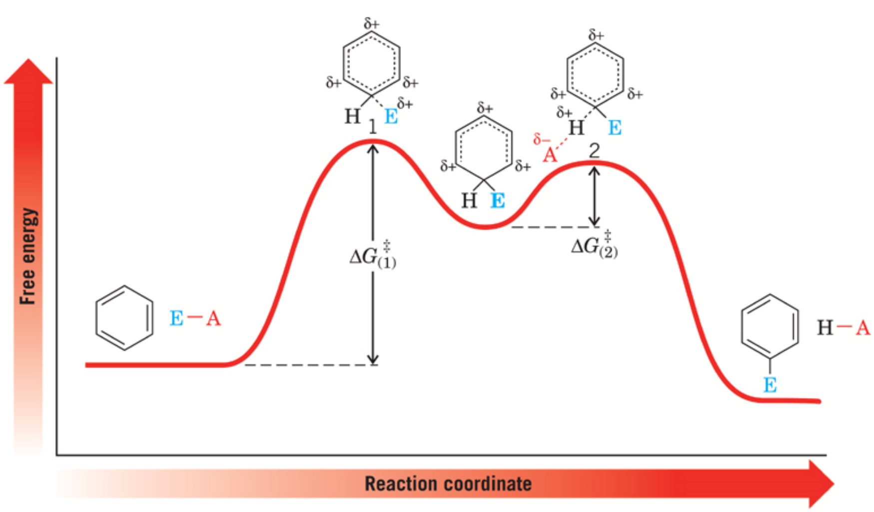
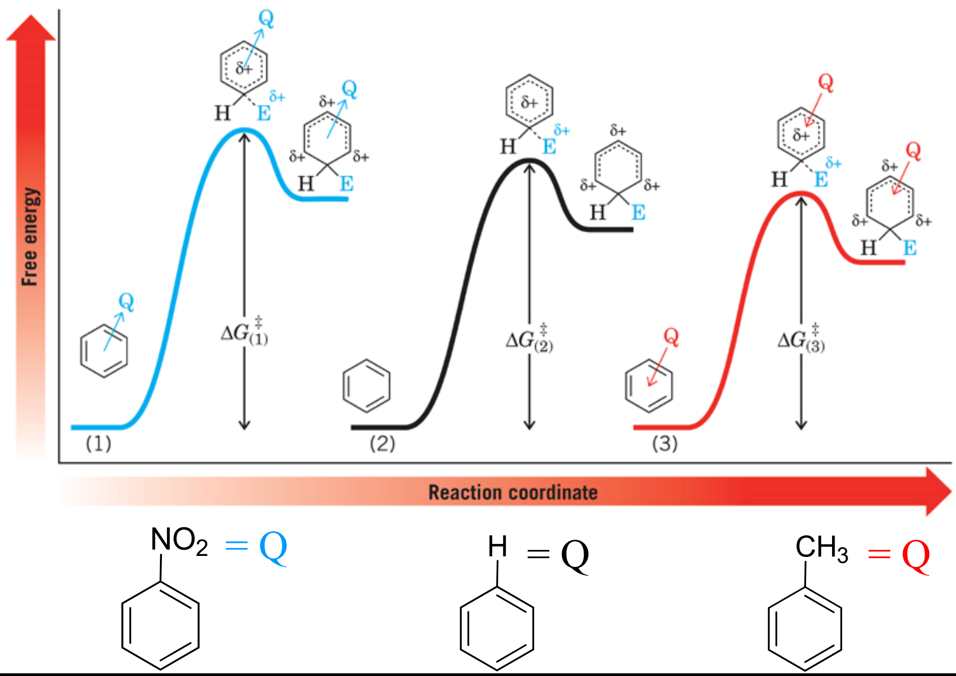


FIGURE 15.3 The free-energy diagram for an electrophilic aromatic substitution reaction. The arenium ion is a true intermediate lying between transition states 1 and 2. In transition state 1 the bond between the electrophile and one carbon atom of the benzene ring is only partially formed. In transition state 2 the bond between the same benzene carbon atom and its hydrogen atom is partially broken. The bond between the hydrogen atom and the conjugate base is partially formed.

EAS R.D.S.: EWG vs. H vs. EDG



Directing Effects in EAS Reactions

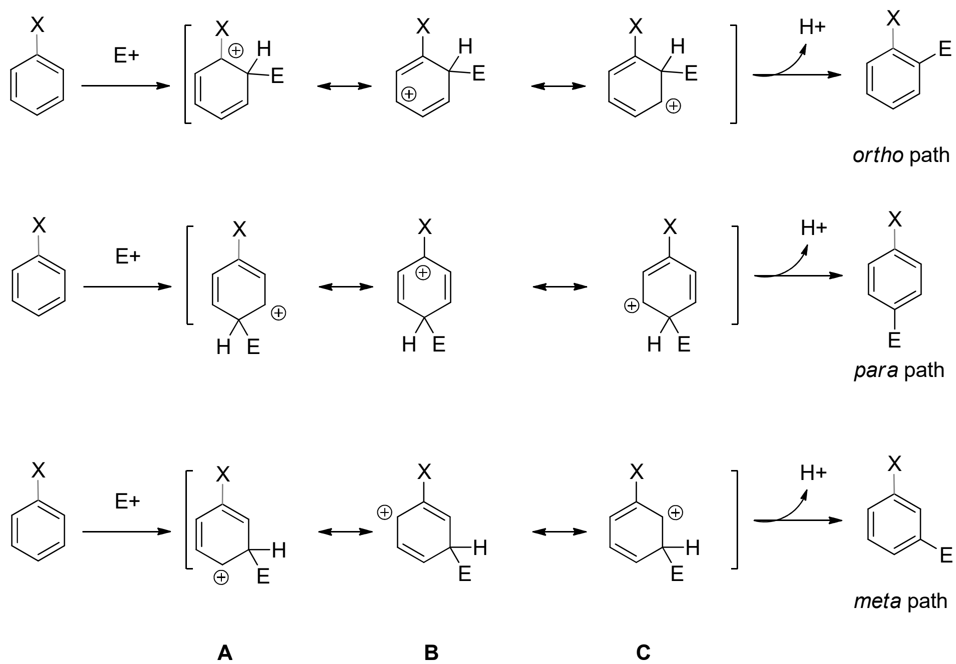
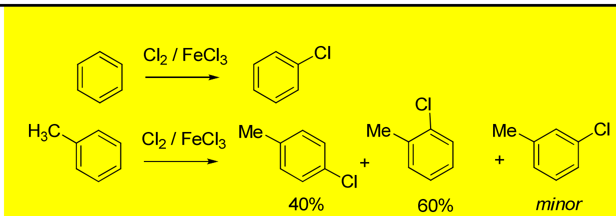


Table 15.2 is Your Friend

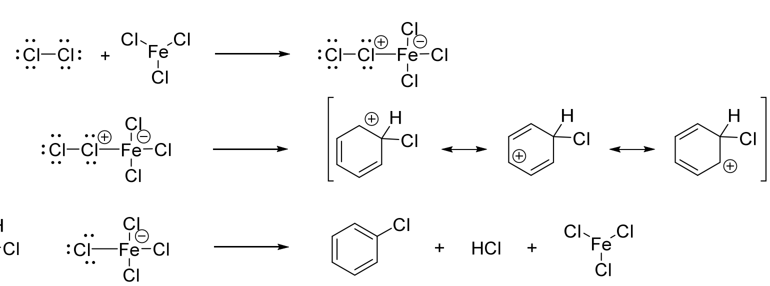
TABLE 15.2 Effect of Substituents on Electrophilic Aromatic Substitution

Ortho–Para Directors	Meta Directors
Strongly Activating	**Moderately Deactivating**
$-NH_2$, $-NHR$, $-NR_2$	$-C\equiv N$
$-OH$, $-O:^-$	$-SO_3H$
Moderately Activating	$-CO_2H$, $-CO_2R$
$-NHCOCH_3$, $-NHCOR$	$-CHO$, $-COR$
$-OCH_3$, $-OR$	**Strongly Deactivating**
Weakly Activating	$-NO_2$
$-CH_3$, $-C_2H_5$, $-R$	$-NR_3^+$
$-C_6H_5$	$-CF_3$, $-CCl_3$
Weakly Deactivating	
$-F:$, $-Cl:$, $-Br:$, $-I:$	

EAS Halogenation



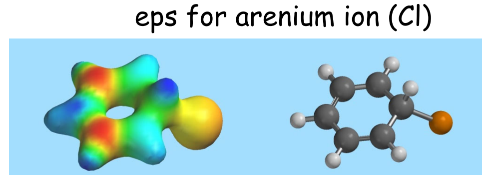
Mechanism:



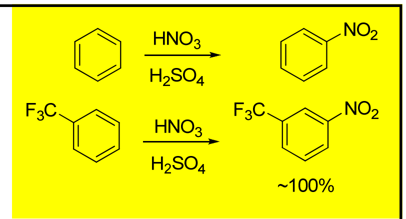
Bromination, use $Br_2/FeBr_3$
(mechanism identical as above)

Iodination, use I_2/HNO_3
(forms I+ by oxidation of I_2)

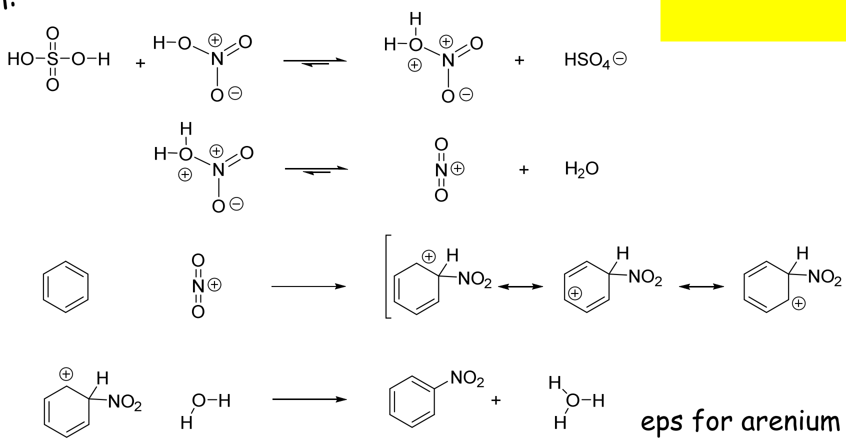
eps for arenium ion (Cl)

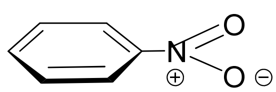


EAS Nitration



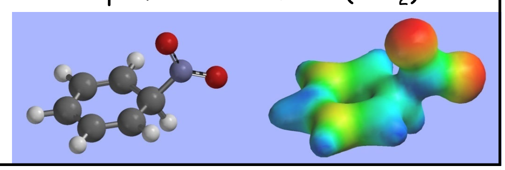
Mechanism:



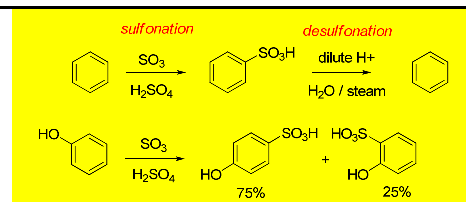


nitrobenzene

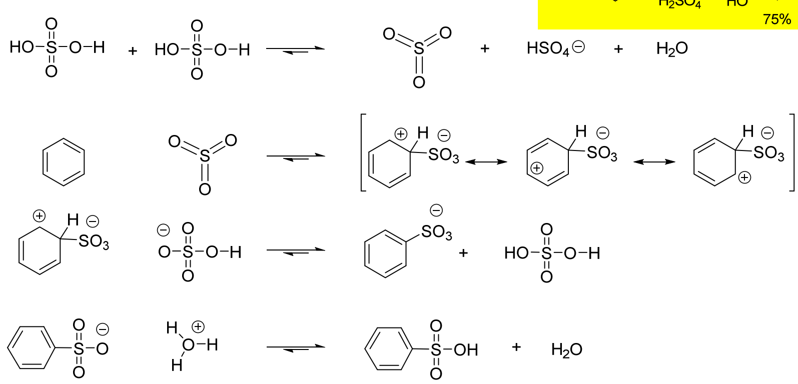
eps for arenium ion (NO_2)



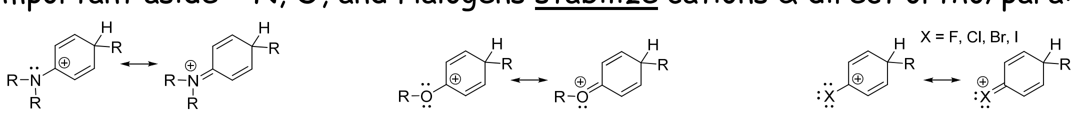
EAS Sulfonation



Mechanism:



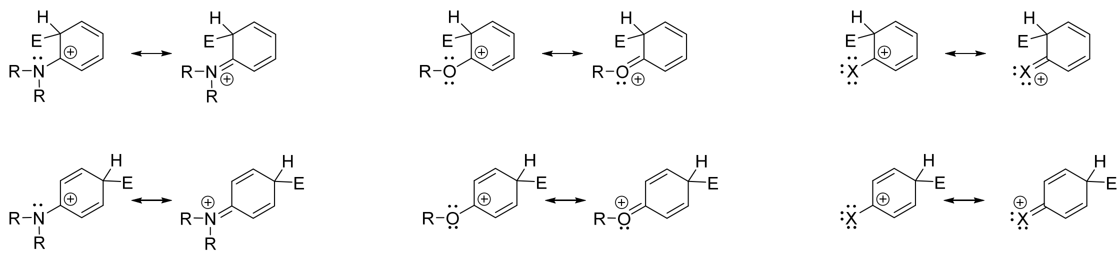
An important aside-- N, O, and Halogens stabilize cations & direct ortho/para:



Great! Good! OK. F is best.

Lone Pairs are important!

N, O, and Halogens stabilize cations & direct ortho/para:



X = F, Cl, Br, I

Cation stabilization: Great!
EAS rate enhanced

Cation stabilization: Good!
EAS rate enhanced

Cation stabilization: OK (F best)
EAS rate slows