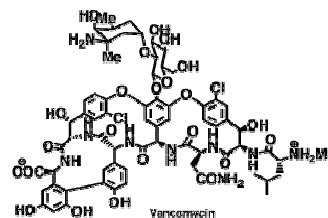
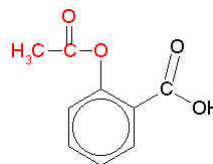
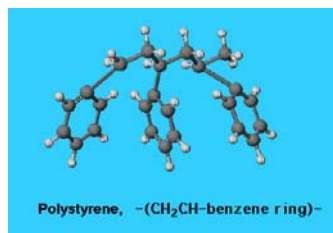
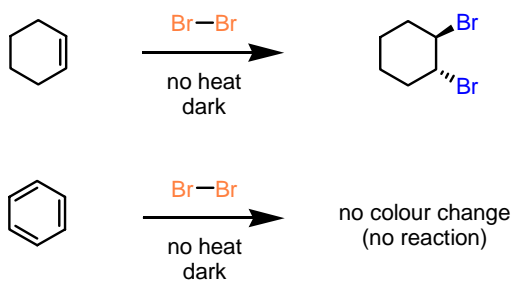


Chapter 12 - Reactions of Benzene - EAS

- 12.1 Introduction to benzene vs. alkenes
- 12.2 Mechanistic principles of *Electrophilic Aromatic Substitution*
- 12.3 Nitration of benzene, reduction to aminobenzenes
- 12.4 Sulfonation of benzene
- 12.5 Halogenation of benzene
- 12.6 Friedel-Crafts alkylation of benzene
- 12.7 Friedel-Crafts alkylation of benzene
- 12.8 Alkylbenzenes via acylation then reduction
- 12.9 Rate and regioselectivity in EAS
- 12.10 Nitration of toluene - rate and regioselectivity
- 12.11 Nitration of CF_3 -benzene - rate and regioselectivity
- 12.12 Substituent effects in EAS: *Activating Substituents*
- 12.13 Substituent effects in EAS: *Strongly Deactivating Substituents*
- 12.14 Substituent effects in EAS: *Halogens*
- 12.15 Multiple substituent effects in EAS
- 12.16 Regioselective synthesis of disubstituted aromatic compounds
- 12.17 Substitution in Naphthalene
- 12.18 Substitution in heterocyclic aromatic compounds



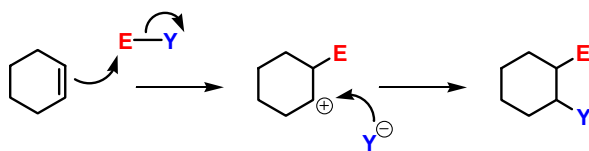
Introduction – Benzene vs. Alkenes



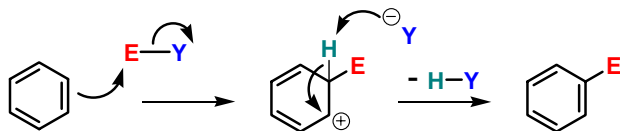
Completely delocalized (6) pi system lends stability (*aromatic*)

12.2 Mechanistic Principles of EAS

Alkenes react by addition



Benzene reacts by substitution



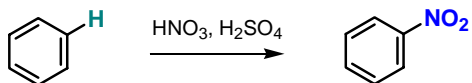
Resonance-stabilized cation

General Mechanism of EAS on Benzene

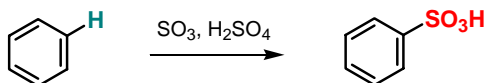
Energy diagram for EAS in benzene
Figure 12.1

Electrophilic Aromatic Substitutions on Benzene

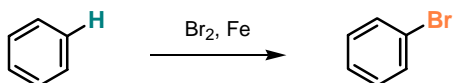
12.3 Nitration



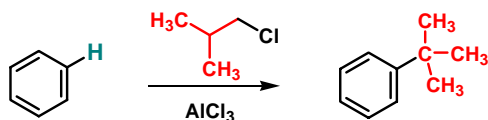
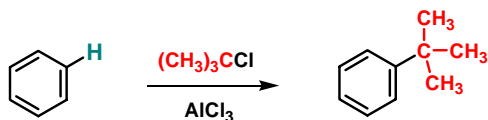
12.4 Sulfonation



12.5 Halogenation



12.6 Friedel-Crafts Alkylation of Benzene

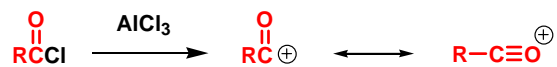
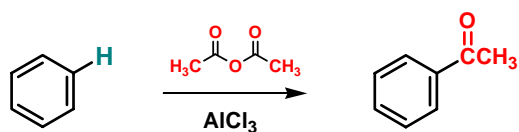
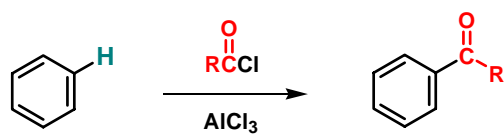


Problems: Alkyl groups may rearrange during reaction

Products are more reactive than benzene

Uses: Alkyl benzenes readily oxidized to benzoic acids using KMnO_4

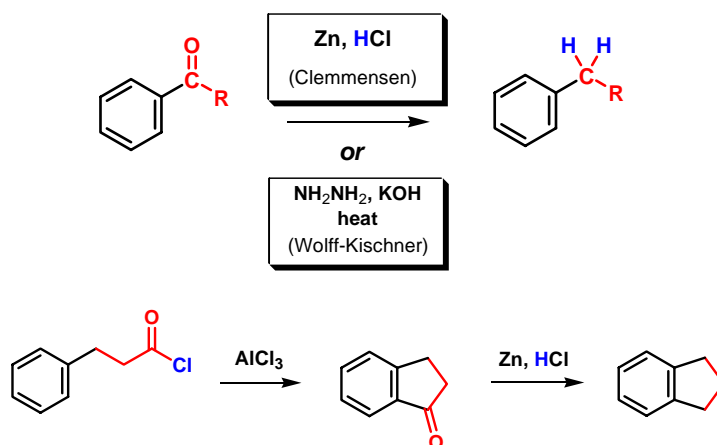
12.7 Friedel-Crafts Acylation of Benzene



Products *react more slowly* than benzene - cleaner reaction

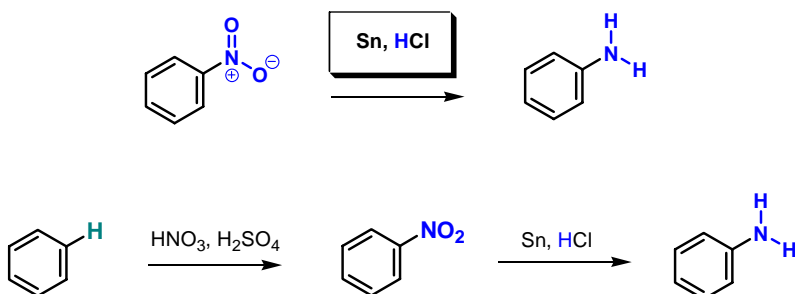
No carbocation rearrangements

12.8 Alkylbenzenes via Acylation/Reduction



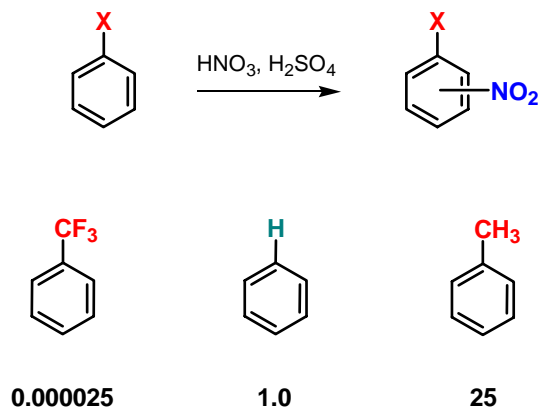
Make the acyl benzene first (clean, high yielding reaction)
 Reduce the ketone group down to the methylene ($\text{C}=\text{O}$ to CH_2)
 Avoids rearrangement problems, better yields

Aminobenzenes via Nitration/Reduction (not in text)



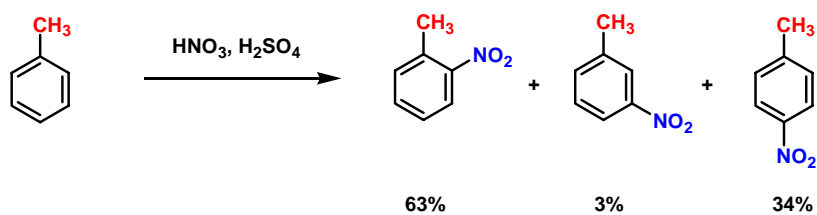
Make the nitro benzene first, clean high yielding reaction
 Reduce the nitro group down to the amine
 Difficult to introduce the amino group by other methods

12.9 Activation and Deactivation by Substituents (Rates)

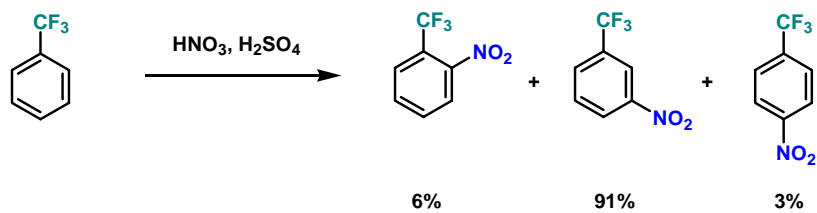


Relative rates in nitration reaction
now bringing in a second substituent

12.9 Nitration of Toluene vs Nitration of (Trifluoromethyl)benzene



CH₃ is said to be an *ortho/para director* (*o/p director*) - *Regioselectivity*



CF₃ is said to be a *meta director* (*m director*) - *Regioselectivity*

12.10 Rate and Regioselectivity in Nitration of Toluene

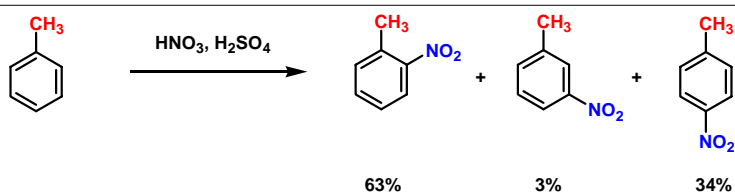


Fig. 12.5 – Energy diagrams for toluene nitration (vs. benzene)

12.11 Rate and Regioselectivity in Nitration of $\text{CF}_3\text{C}_6\text{H}_5$

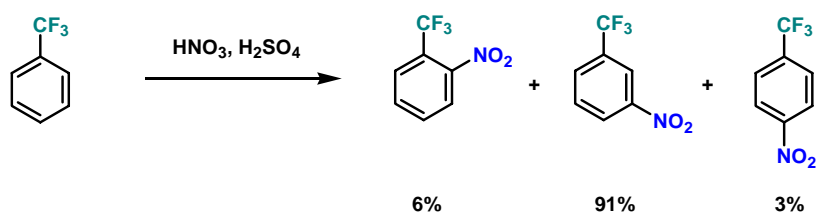
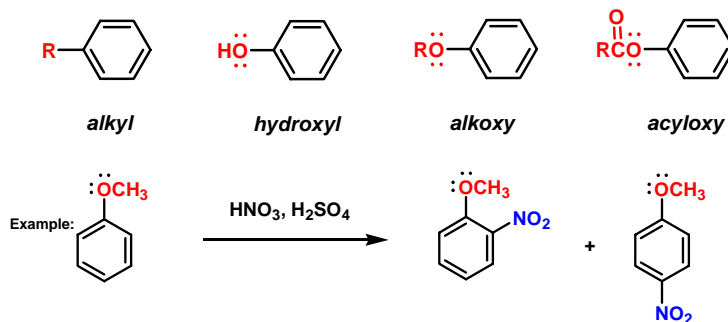


Fig. 12.6 – Energy diagrams for $\text{CF}_3\text{C}_6\text{H}_5$ nitration (vs. benzene)

12.12 Substituent Effects – Activating Substituents

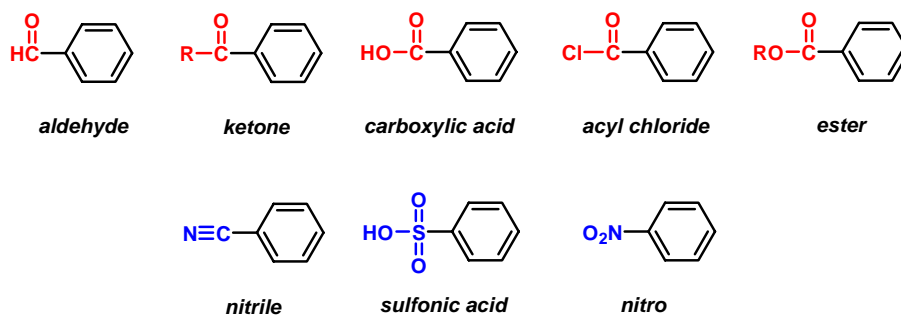
General : all activating groups are *o/p* directors
 halogens are slightly deactivating but are *o/p* directors
 strongly deactivating groups are *m* directors

Activating Substituents



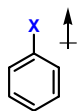
Alkyl groups stabilize carbocation *by hyperconjugation*
 Lone pairs on O (and others like N) *stabilize by resonance*

12.13 Subst. Effects – Strongly Deactivating Substituents

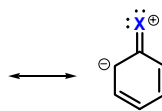
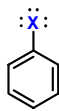


Second substituent goes *meta by default* – best carbocation

12.14 Substituent Effects – Halogens



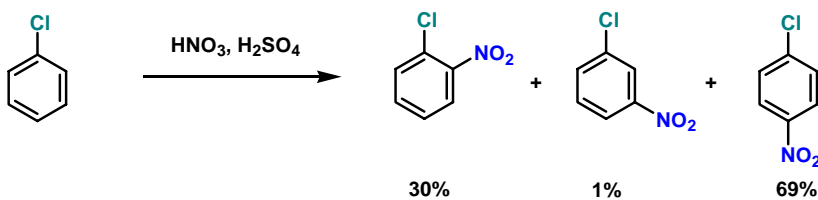
X = F, Cl, Br



X = F, Cl, Br

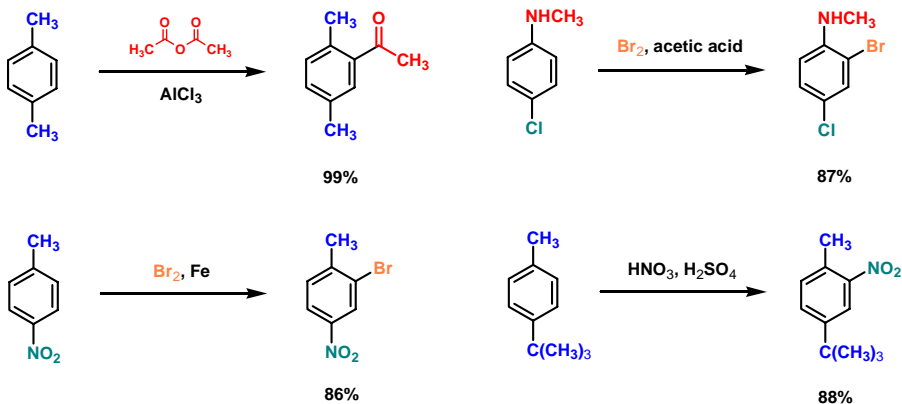
Reactivity (i.e. rate) is a balance between inductive effect (EW) and resonance effect (ED) – larger Cl, Br, I do not push lone pair into pi system as well as F, O, N, which are all first row (2p)

Example:



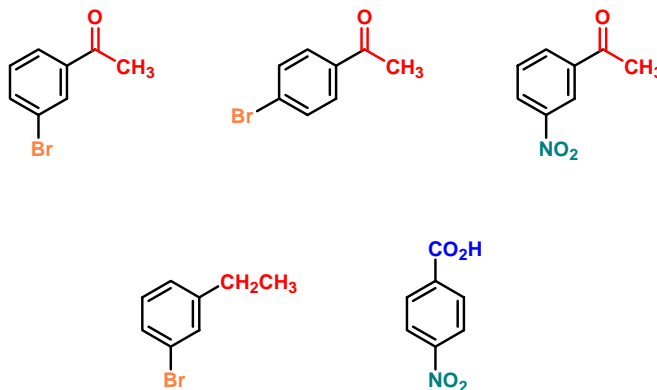
Regioselectivity - second substituent goes *o/p* – *better carbocations*

12.15 Multiple Substituent Effects



Interplay between power of directing group and size of substituents

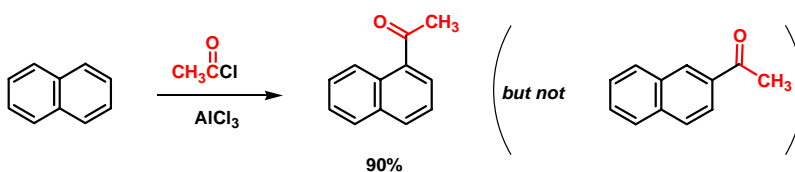
12.16 Regioselective Synthesis of Disubstituted Derivs.



Have to be careful about when to introduce each substituent
Remember – isomers (e.g. *o/p* mixtures) may be separated

12.17-12.18 Substitution in Other Aromatic Systems

12.17 Naphthalene



12.18 Heterocycles

