Organic Chemistry

5th Edition

Paula Yurkanis Bruice

Chlorobenzene

meta-Bromobenzoic acid

ortho-Chloronitrobenzene

para-Iodobenzenesulfonic acid

Chapter 15

Reactions of Substituted Benzenes

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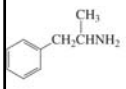
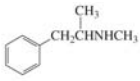
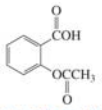
Examples of Substituted Benzenes



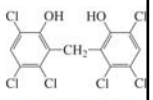
amphetamine
an appetite suppressant



methamphetamine
"speed"



acetylsalicylic acid
aspirin



hexachlorophene
a disinfectant

Nomenclature of Substituted Benzenes

In disubstituted benzenes, the relative positions of the two substituents are indicated by numbers or by prefixes

1,2-dibromobenzene
ortho-dibromobenzene
o-dibromobenzene

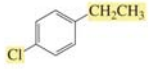
1,3-dibromobenzene
meta-dibromobenzene
m-dibromobenzene

1,4-dibromobenzene
para-dibromobenzene
p-dibromobenzene

The two substituents are listed in alphabetical order

1-chloro-3-iodobenzene
meta-chloroiodobenzene
not
1-iodo-3-chlorobenzene or
meta-iodochlorobenzene

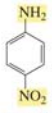
1-bromo-3-nitrobenzene
meta-bromonitrobenzene



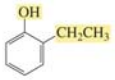
1-chloro-4-ethylbenzene
para-chloroethylbenzene

If one of the substituents can be incorporated into a name, that name is used and the incorporated substituent is given the 1-position

2-chlorotoluene
ortho-chlorotoluene
not
ortho-chloromethylbenzene

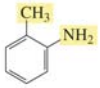


4-nitroaniline
para-nitroaniline
not
para-aminonitrobenzene



2-ethylphenol
ortho-ethylphenol
not
ortho-ethylhydroxybenzene

Some disubstituted benzenes have names that incorporate both substituents



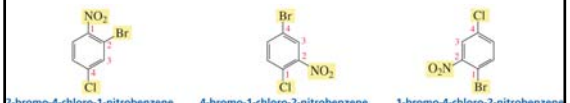
ortho-toluidine

meta-xylene

para-cresol
used as a wood preservative until prohibited for environmental reasons

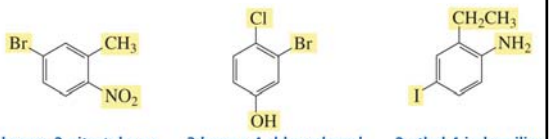
Naming Polysubstituted Benzenes

The substituents are numbered in the direction that results in the lowest possible number



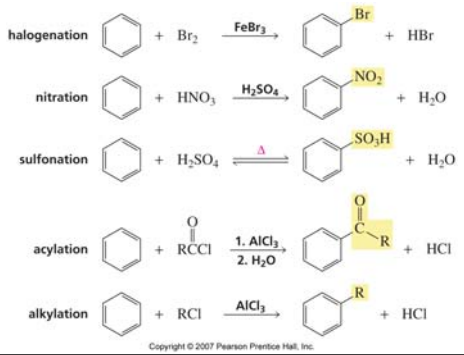
2-bromo-4-chloro-1-nitrobenzene 4-bromo-1-chloro-2-nitrobenzene 1-bromo-4-chloro-2-nitrobenzene

The incorporated substituent is given the 1-position; the ring is numbered in the direction that yields the lowest possible number



5-bromo-2-nitrotoluene 3-bromo-4-chlorophenol 2-ethyl-4-iodoaniline

Substituted benzenes undergo the five electrophilic aromatic substitution reactions discussed in Chapter 14



The slow step of an electrophilic aromatic substitution reaction is the formation of the cation intermediate

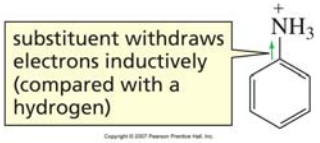
Electron-donating substituents increase the rate of the substitution reactions by stabilizing the carbocation intermediate and the transition state leading to its formation

Electron-donating groups are activating substituents

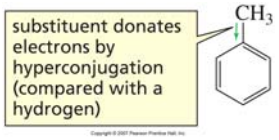
Electron-withdrawing groups are deactivating substituents

relative rates of electrophilic aromatic substitution

Inductive Electron Withdrawal



Electron Donation by Hyperconjugation



Donation of electrons through a σ bond is called inductive electron donation

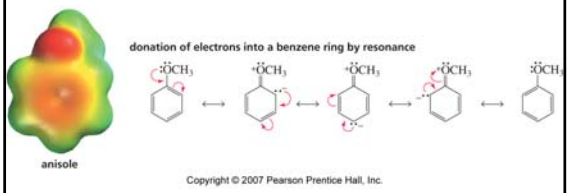
An alkyl group is more electron donating than hydrogen because of hyperconjugation

Withdrawal of electrons through a σ bond is called inductive electron withdrawal

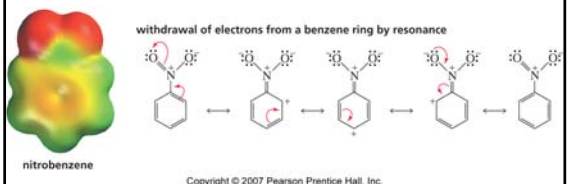
The NH_3 group is more electronegative than a hydrogen

Resonance Electron Donation and Withdrawal

Substituents such as NH_2, OH, OR, and Cl donate electrons by resonance; they also withdraw electrons inductively

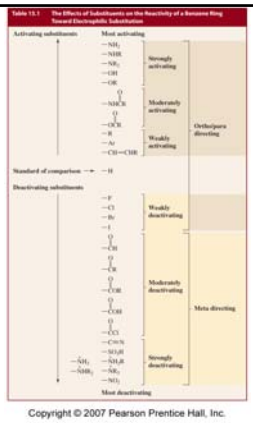


Substituents such as C=O, C≡N, SO_3H, and NO_2H withdraw electrons by resonance; they delocalize the π electrons of the ring onto the substituents



Electron-donating substituents increase the reactivity of the benzene ring toward electrophilic aromatic substitution

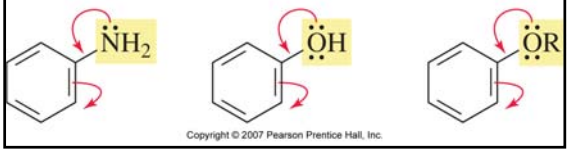
Electron-withdrawing substituents decrease the reactivity of the benzene ring toward electrophilic aromatic substitution



The strongly activating substituents make the benzene ring more reactive toward electrophilic substitution

Electron donation into the ring by resonance is more significant than their inductive electron withdrawal from the ring

strongly activating substituents

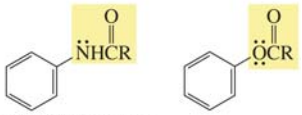


The moderately activating substituents donate electrons into the ring by resonance and withdraw electrons inductively

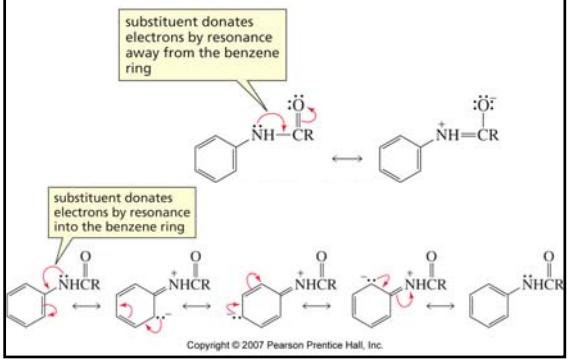
The substituents can donate electrons into the ring and away from the ring

Overall, they donate electrons by resonance more strongly than they withdraw electrons inductively

moderately activating substituents

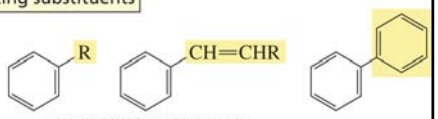


These substituents are less effective in donating electrons into the ring because…



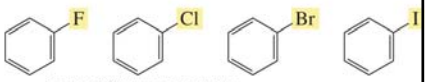
Alkyl, aryl, and CH=CHR groups are weakly activating substituents because they are slightly more electron donating than they are electron withdrawing

weakly activating substituents



These substituents donate into the ring by resonance and withdraw electrons from the ring inductively

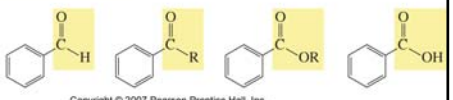
weakly deactivating substituents



They withdraw electrons inductively more strongly than they donate electrons by resonance

These substituents withdraw electrons both inductively and by resonance

moderately deactivating substituents

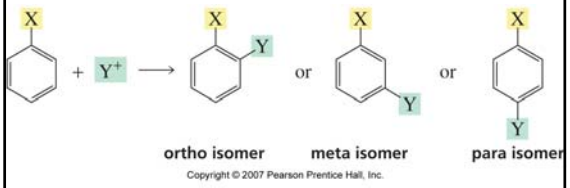


These substituents are powerful electron-withdrawing groups

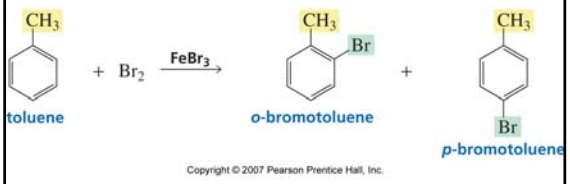
Except for the ammonium ions, these substituents withdraw electrons both inductively and by resonance

strongly deactivating substituents

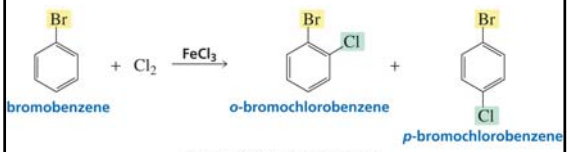
The substituent already attached to the benzene ring determines the location of the new substituent



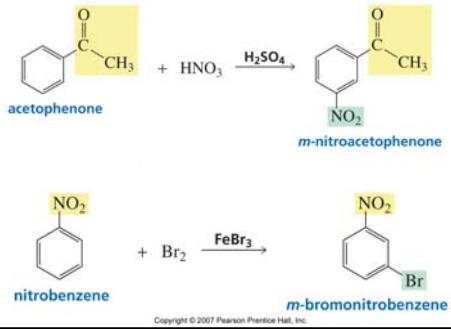
All activating substituents are ortho–para directors



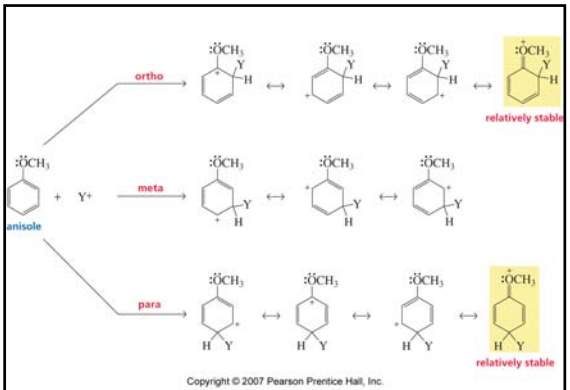
The weakly deactivating halogens are ortho–para directors

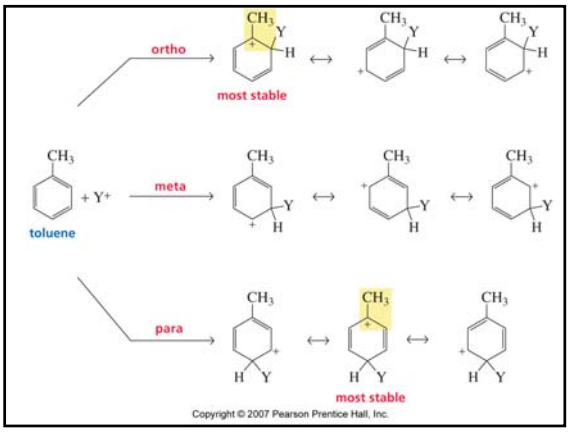


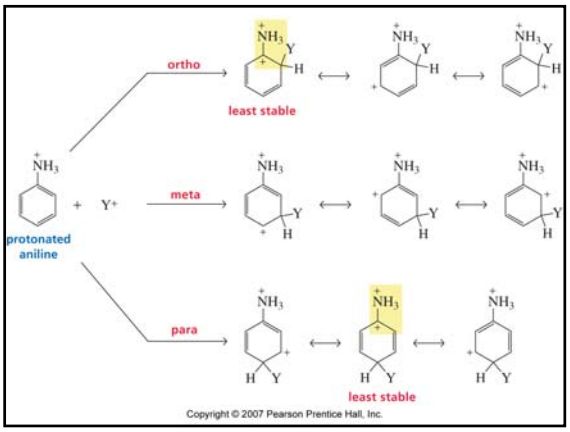
All substituents that are more deactivating than halogens are meta directors



- The relative stabilities of the carbocations formed from the electrophilic substitution of the substituted benzene determine the preferred reaction pathway
- All substituents that donate electrons either by resonance or by hyperconjugation is an ortho–para director
- All substituents that cannot donate electrons are meta directors



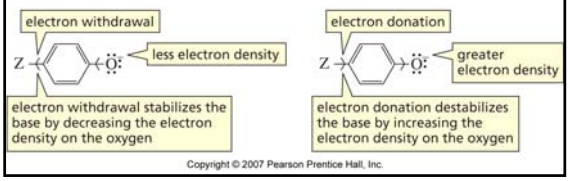


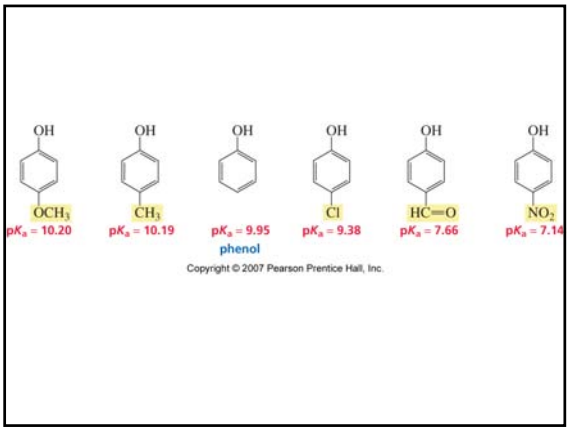


The Effect of Substituents on pK_a

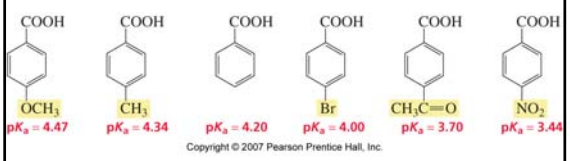
Electron-withdrawing groups stabilize a base and therefore increase the strength of its conjugate acid

Electron-donating groups destabilize a base and this decreases the strength of its conjugate acid

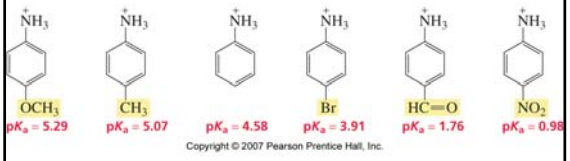




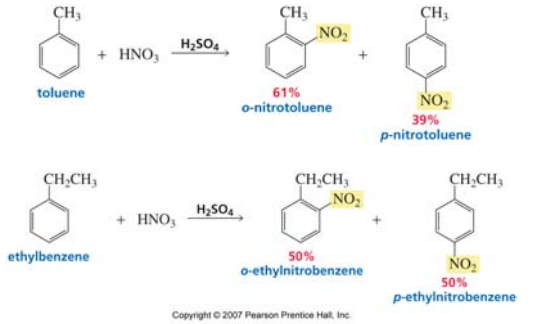
The more deactivating a substituent, the more acidic is the acid attached to the benzene ring

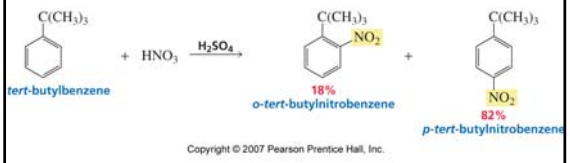


The more activating the substituent, the less acidic is the acid attached to the benzene ring

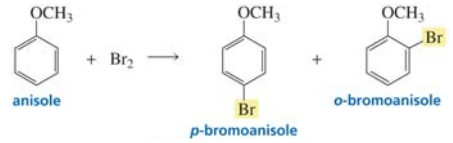


The ortho–para product ratio decreases with an increase in the size of the substituents

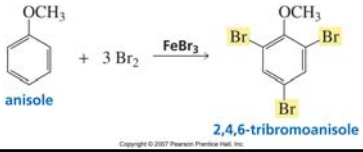




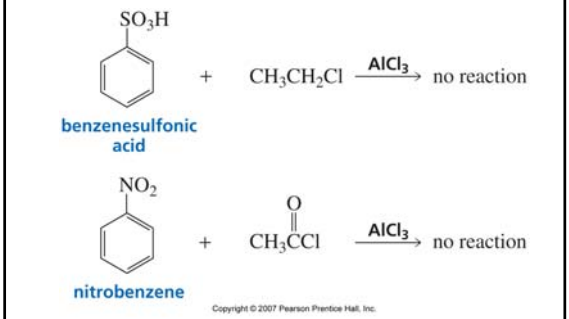
Methoxy and hydroxy substituents are so strongly activating that halogenation is carried out without Lewis



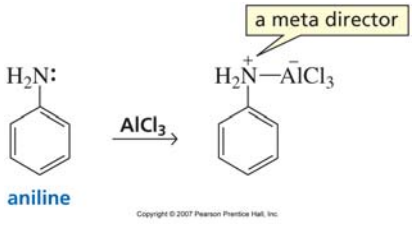
The presence of Lewis acid and excess bromine generates the tribromide



A benzene ring with a meta director cannot undergo a Friedel-Crafts reaction



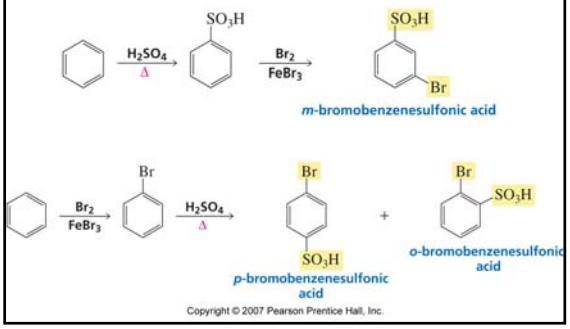
Aniline and *N*-substituted anilines do not undergo Friedel–Crafts reaction



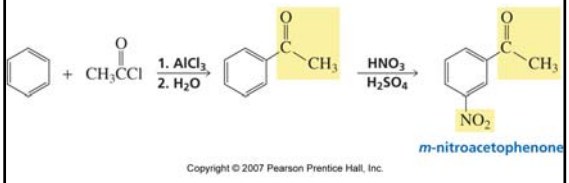
Phenol and anisole undergo Friedel-Crafts reactions at the ortho-para positions

Aniline cannot be nitrated; it can be oxidized by nitric acid

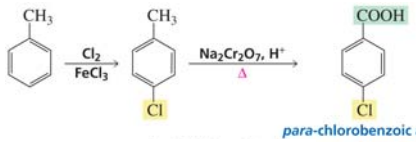
In designing a disubstituted benzene, the order in which the substituents are to be placed on the ring must be considered



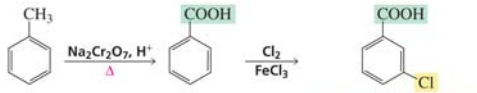
The Friedel-Crafts acylation must be carried out first because the nitro group is strongly deactivating



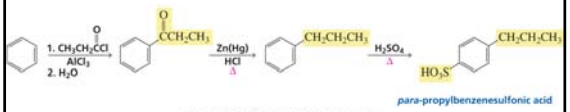
In the synthesis of *para*-chlorobenzoic acid from toluene, the methyl group is oxidized first



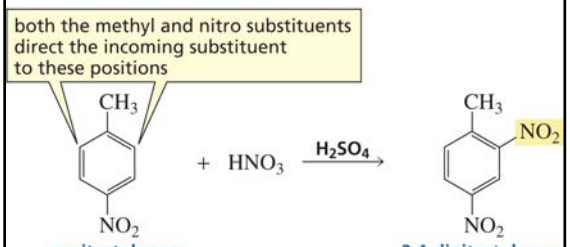
In the synthesis of *meta*-chlorobenzoic acid, the methyl group is oxidized before chlorination

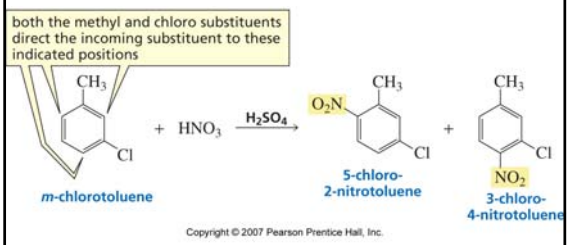


In the following synthesis, the type of reaction used, the order of introducing the substituents, and the point at which a substituent is chemically modified must be considered

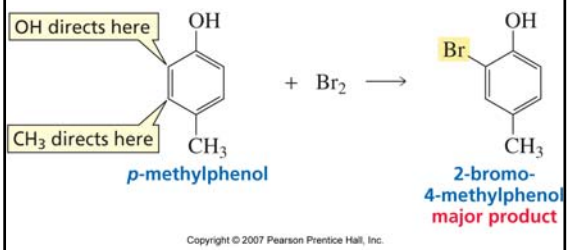


Synthesis of Trisubstituted Benzenes



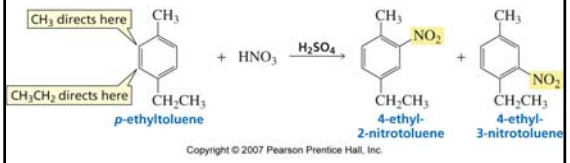


Steric hindrance makes the position between the substituents less accessible

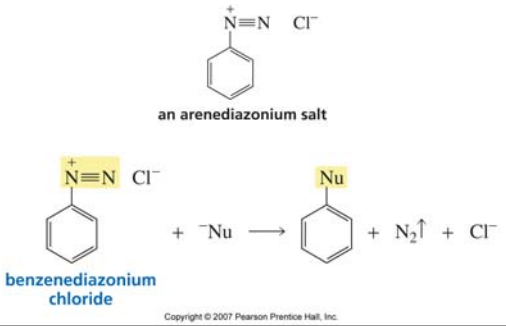


A strongly activating substituent will win out over a weakly activating substituent or a deactivating substituent

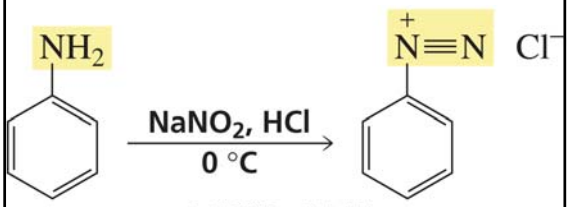
If the two substituents have similar activating properties, neither will dominate



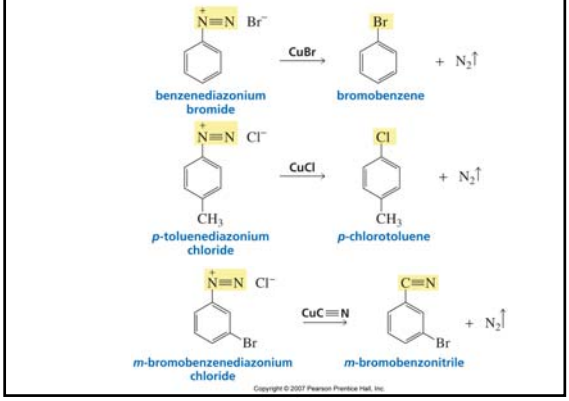
Synthesis of Substituted Benzenes Using Arenediazonium Salts



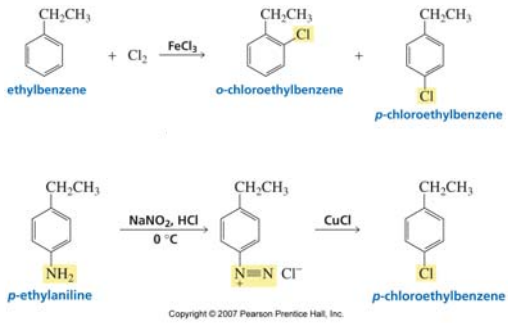
Preparation of the Diazonium Salt

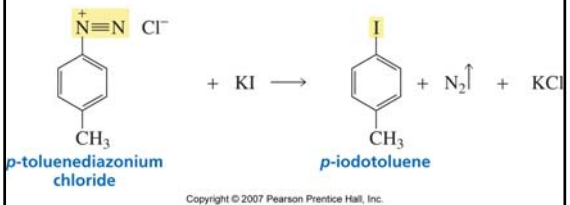


Sandmeyer reactions



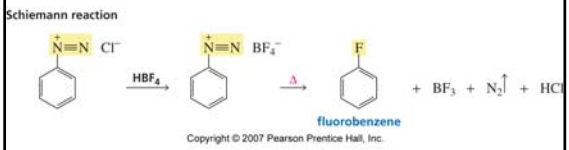
Consider the synthesis of *para*-chloroethylbenzene

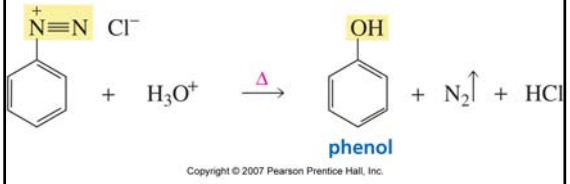




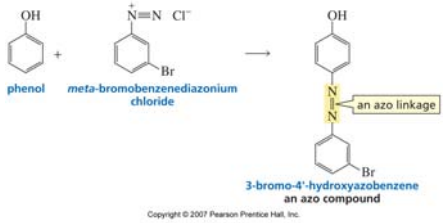
Fluorination of Benzene

Schiemann reaction





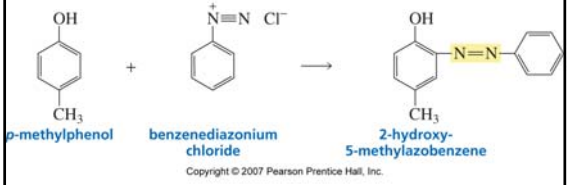
The Arenediazonium Ion as an Electrophile



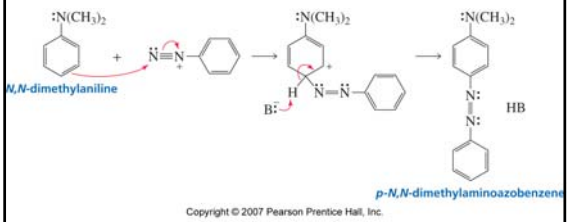
Only highly activated benzene rings can undergo this reaction

Substitution takes place preferentially at the para position

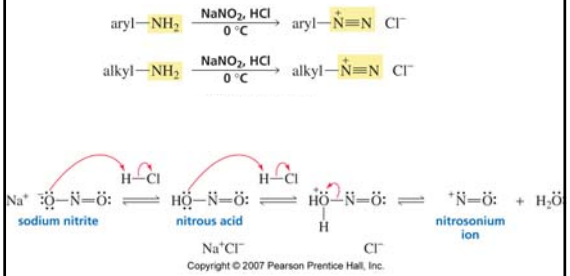
However, if the para position is blocked …

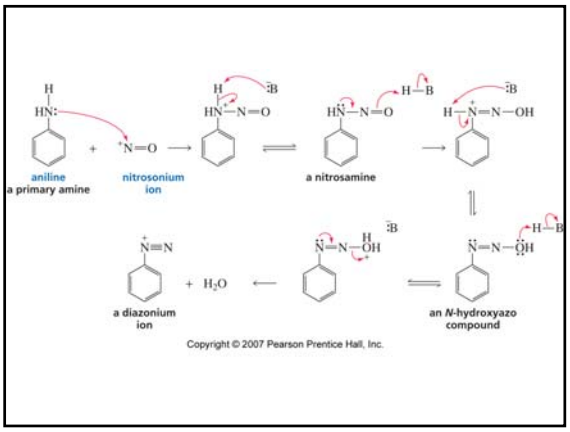


Mechanism

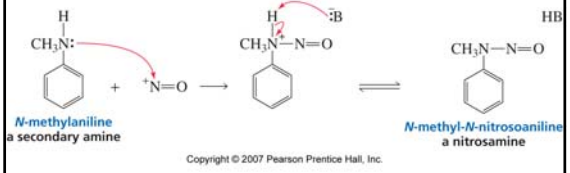


Reaction of Amines with Nitrous Acid

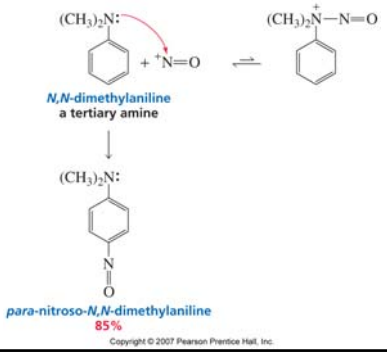




The reaction stops because a secondary amine lacks a second proton

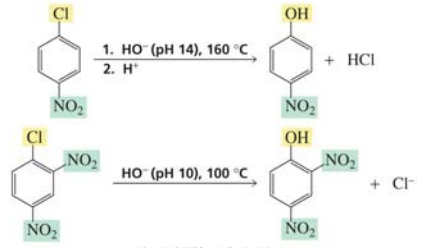


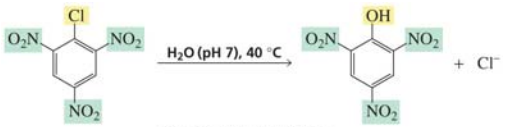
The bulky dialkyl amino group blocks the approach of the nitrosonium ion to the ortho position



Nucleophilic Aromatic Substitution Reactions

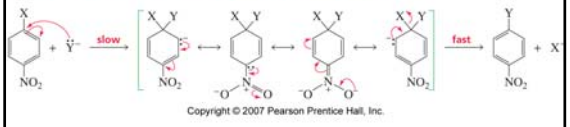
Nucleophilic aromatic substitution reactions can occur when an aryl halides have at least one strongly electron-withdrawing substituent attached to the benzene ring



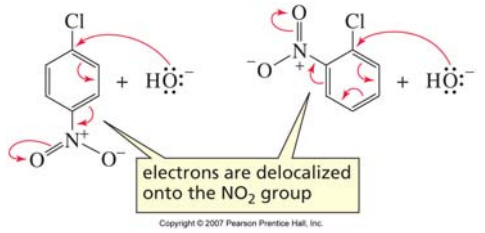


Electron-withdrawing substituents increase the reactivity of the benzene ring toward nucleophilic substitution and decrease the reactivity of the benzene ring toward electrophilic substitution

General mechanism for nucleophilic aromatic substitution

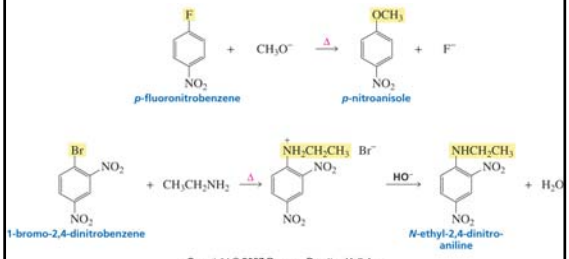


The electron-withdrawing substituents must be ortho or para to the site of nucleophile attack

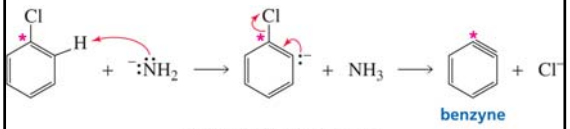


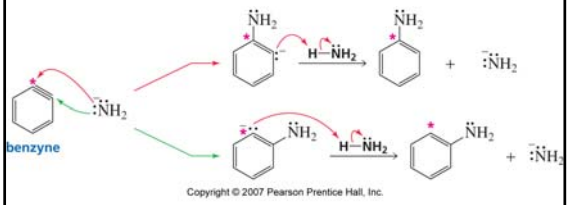
The electrons of the attacking nucleophile can be delocalized

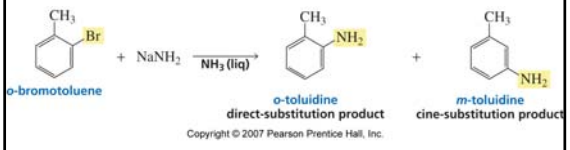
The incoming group has to be a stronger base than the group that is being replaced



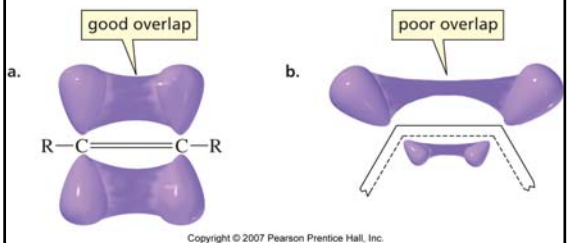
Formation of Benzyne







Benzyne Is an Extremely Reactive Species



Polycyclic Benzoid Hydrocarbons