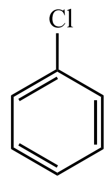
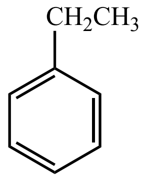
Chapter 19: Benzene and Aromatic Substitution Reactions

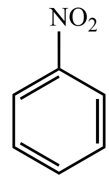
[Sections: 18.2, 18.6; 19.1-19.12]

Nomenclature of Substituted Benzenes

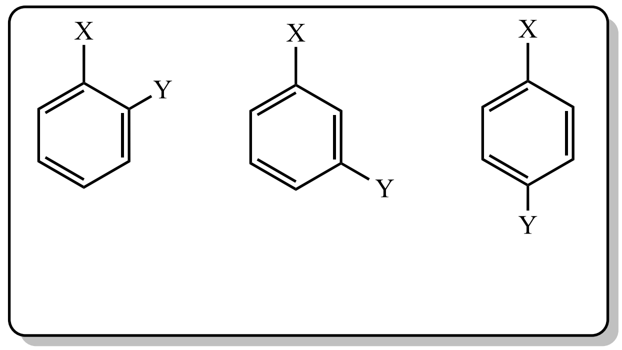
i. Monosubstituted Benzenes

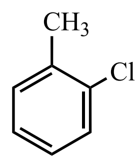


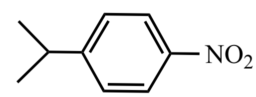




ii. Disubstituted Benzenes



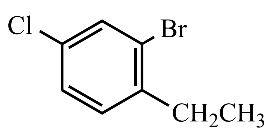




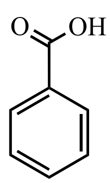
• with 2 substituents, either the *ortho*, *meta*, *para*-terminology OR locant values may be used

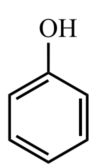
iii. Polysubstituted Benzenes

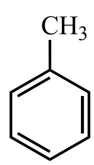
- with more than 2 substituents, locant values MUST be used
- Minimize value of locants
- Name alphabetically

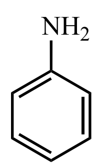


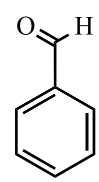
iv. IUPAC Accepted Common Names

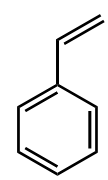


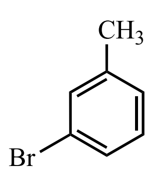




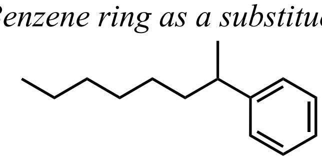


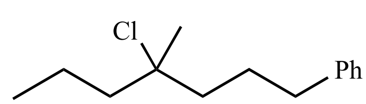






v. Benzene ring as a substituent is a "phenyl" group

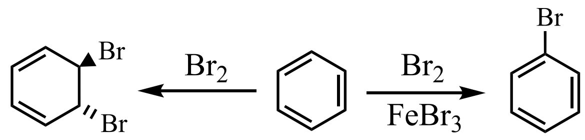




• if a continuous chain attached to a benzene ring exceeds 6 carbons, the benzene ring becomes a substituent off of the parent alkyl chain

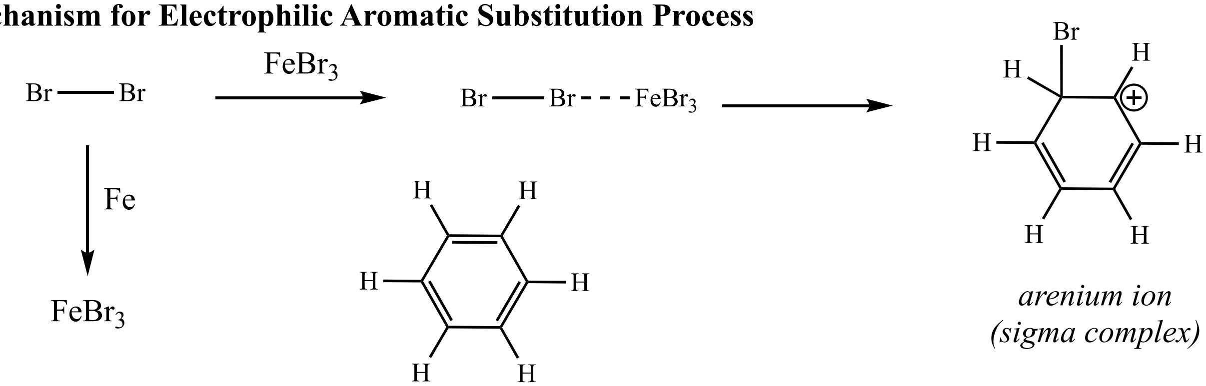
Problems: 1

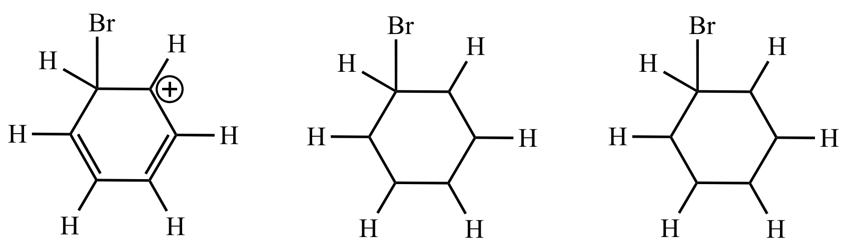
Substitution versus Addition Reactions



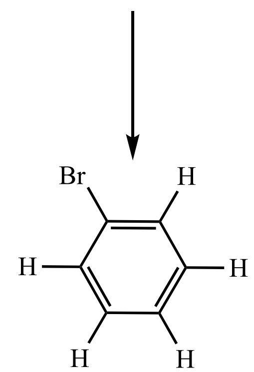
• substitution reactions are favored by aromatic compounds since aromaticity is retained
• addition reactions (typical of alkenes) would result in loss of aromaticity

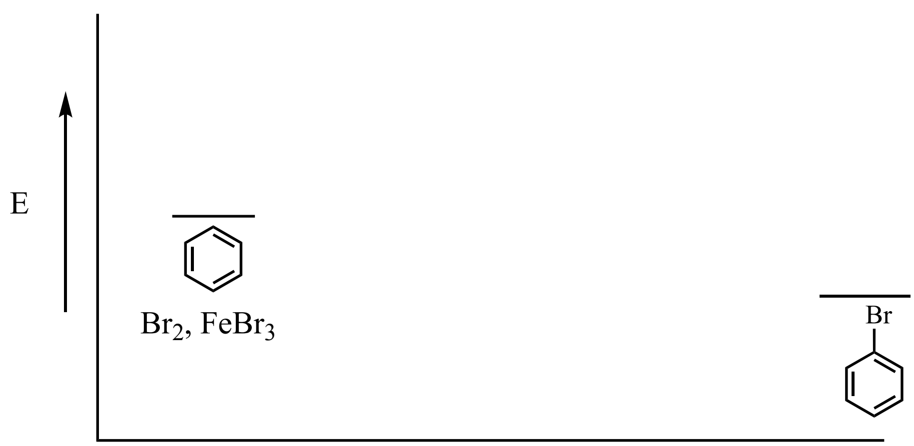
Mechanism for Electrophilic Aromatic Substitution Process





• arenium ion (or sigma complex) intermediate is formed
• resonance stabilization means it has a reasonable activation barrier for formation since aromaticity is temporarily lost

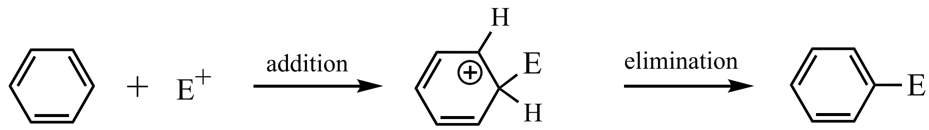




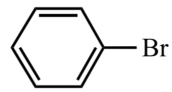
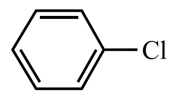
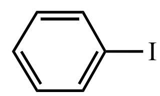
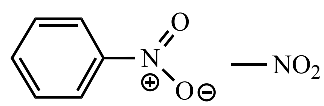
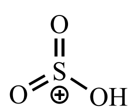
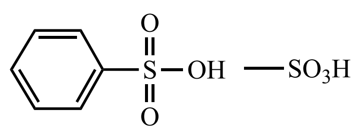
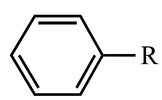
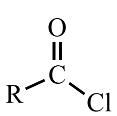
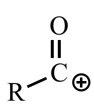
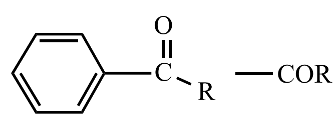
• the net result is substitution on the aromatic ring by an electrophile
• the aromatic ring is able to supply electrons to the electrophile from the pi system
• the process is referred to as "electrophilic aromatic substitution" (EAS for short)

Common Electrophiles that Engage in Electrophilic Aromatic Substitution

- all sufficiently strong electrophiles engage in the two step EAS process, an addition step to form the arenium ion followed by an elimination step to form the aromatic substituted product

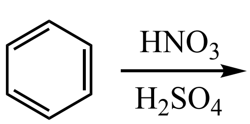


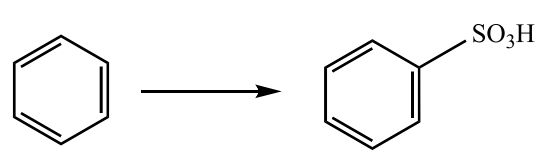
arenium ion
(sigma complex)

Conditions for Generating E^+	Active E^+	Product	Process Name	
Br_2, $FeBr_3$ (or $AlBr_3$)	$\overset{\delta+}{Br}—Br---\overset{\delta-}{FeBr_3}$	 bromobenzene	Bromination	HALOGENATION
Cl_2, $FeCl_3$ (or $AlCl_3$)	$\overset{\delta+}{Cl}—Cl---\overset{\delta-}{FeCl_3}$	 chlorobenzene	Chlorination	HALOGENATION
I_2, $CuCl_2$	"I^+"	 iodobenzene	Iodination	HALOGENATION
H_2SO_4, HNO_3	$O=\overset{\oplus}{N}=O$	 nitrobenzene	Nitration	
H_2SO_4, SO_3		 benzene sulfonic acid	Sulfonation	
R—X, AlX_3 (X=Cl, Br, I)	$R^{\oplus}$	 alkylbenzene	Alkylation (Friedel-Crafts)	
 , $AlCl_3$ acid chloride		 acylbenzene	Acylation (Friedel-Crafts)	

- each set of conditions generates an electrophile (E+) that then reacts with the benzene ring
- you MUST learn the conditions to generate each of the electrophiles and also what product each set of reaction conditions produces

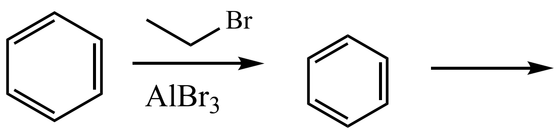
Examples

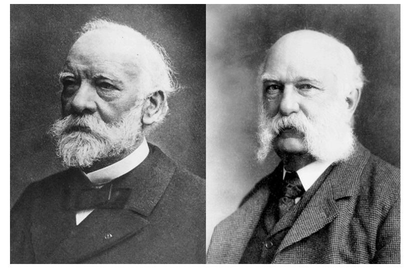




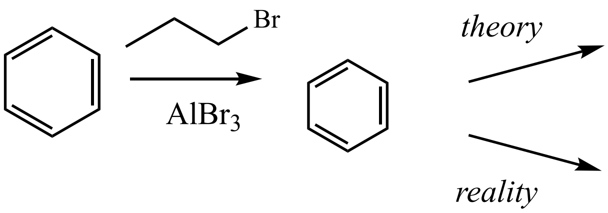
A Limitation on the Friedel-Crafts Reactions

Potential for rearrangements

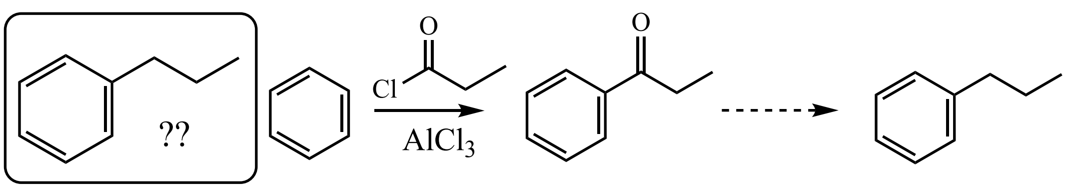




Charles Friedel 1832-1899 | James Crafts 1839-1917



• in the Friedel-Crafts alkylation reaction, as in any reaction involving a carbocation intermediate, rearrangement to a more stable carbocation is expected
• this is a limitation to the reaction that often prevents straight-chain alkyl groups from being substituted onto aromatic rings in a single step



• the Friedel-Crafts acylation reaction does NOT have competing rearrangements
• if the carbonyl group could be converted to a CH_2 group, this is a way to substitute straight-chain alkyl groups onto an aromatic ring using a two-step method
• this is considered to be a "reduction" reaction since hydrogen is added to the molecule

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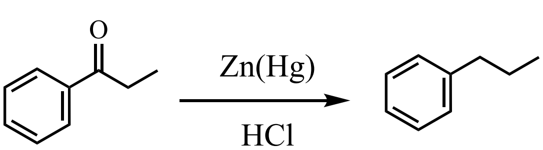
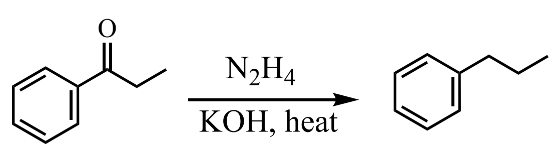
Clemmensen Reduction



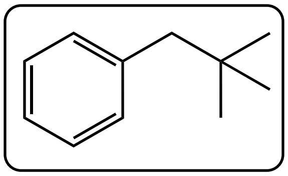
• an "amalgam" of zinc and mercury metal in the presence of strongly acidic HCl will reduce a carbonyl group to a CH_2

Wolff-Kishner Reduction



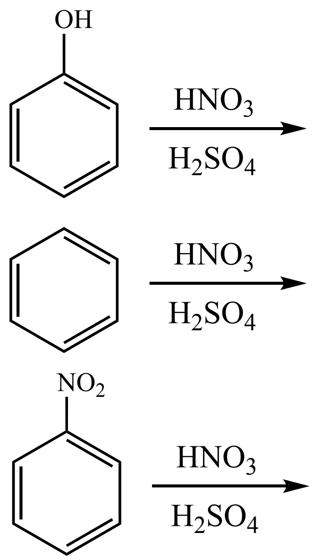
• heating hydrazine (H_2NNH_2) in the presence of strongly basic KOH will reduce a carbonyl group to a CH_2

Example



Problems: 2

Effects of Substituents Already on the Benzene Ring

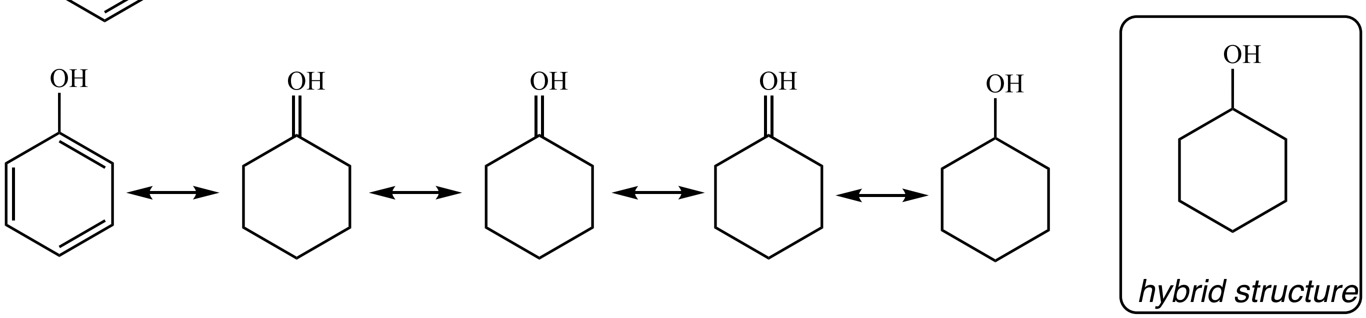


rate = 1000 X faster

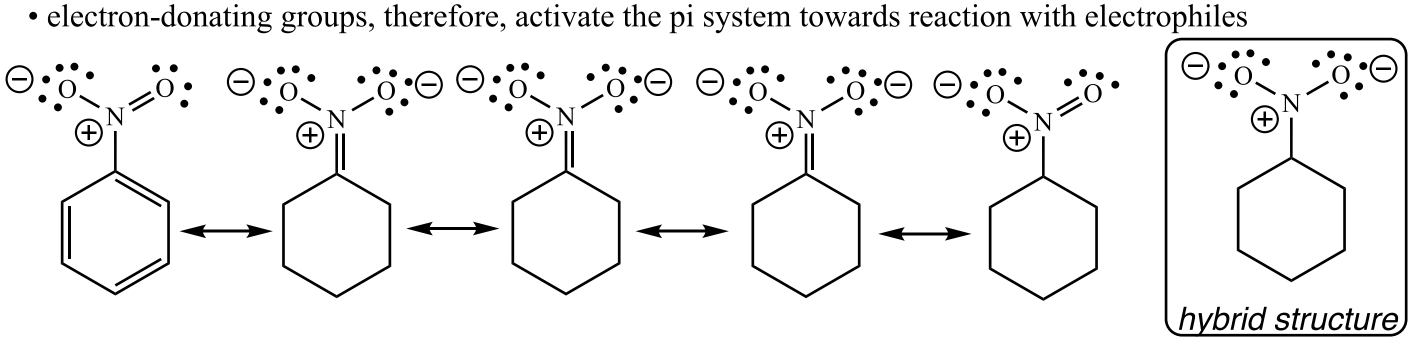
rate = 1

rate = 100 million times slower

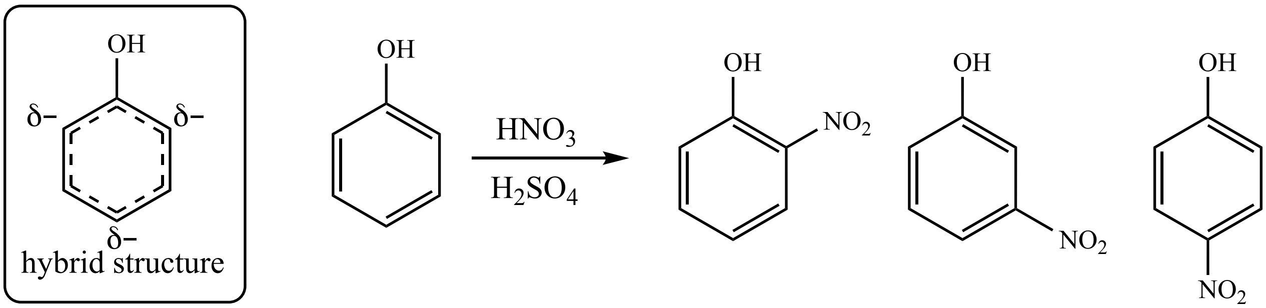
- some substituents will increase the rate of reaction of an aromatic ring with electrophiles compared to the rate of unsubstituted benzene
- these substituents are considered to be "activators"
- some substituents will decrease the rate of reaction of an aromatic ring with electrophiles compared to the rate of unsubstituted benzene
- these substituents are considered to be "deactivators"

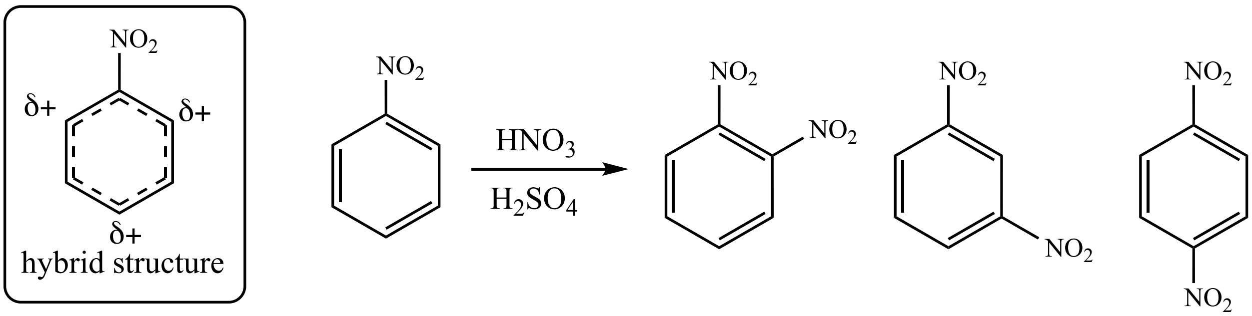


- the OH substituent increases the electron density of the aromatic pi system by donating electrons to the ring via resonance
- the OH substituent is termed an "electron-donating" group or an "electron-donor"
- the increased electron density results in faster reaction with electrophiles
- electron-donating groups, therefore, activate the pi system towards reaction with electrophiles



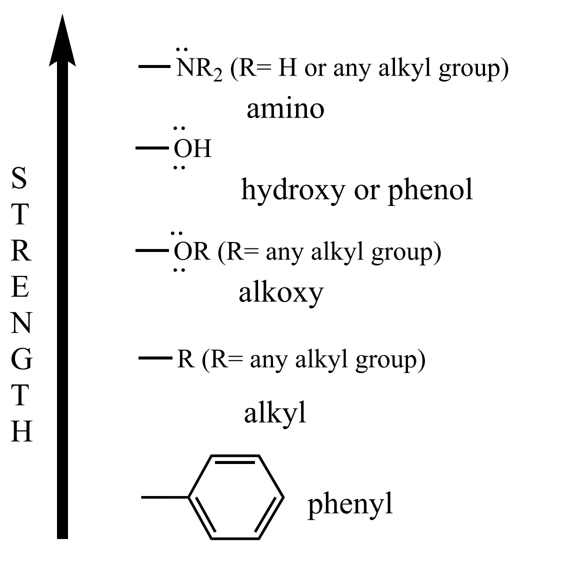
- the NO_2 substituent decreases the electron density of the aromatic pi system by withdrawing electrons from the ring via resonance
- the NO_2 substituent is termed an "electron-withdrawing" group
- the decreased electron density results in slower reaction with electrophiles
- electron-withdrawing groups, therefore, deactivate the pi system towards reaction with electrophiles





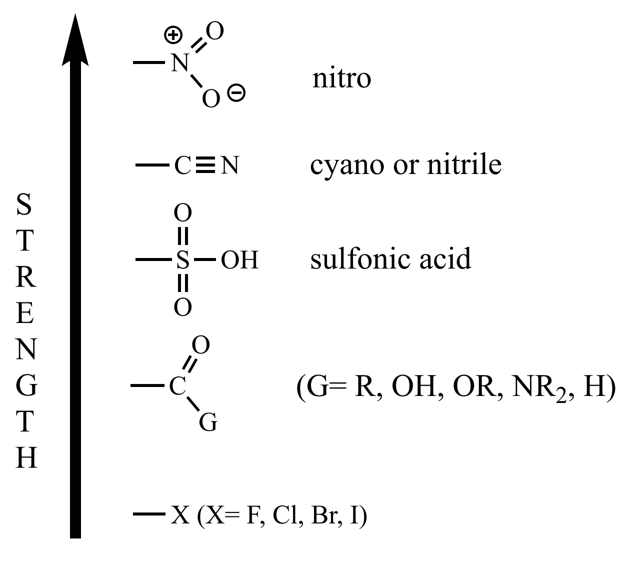
- the effect of the electron-donating OH group is to build up electron density at the ortho and para positions of the ring. The electrophile reacts preferentially at those positions since those are the most electron rich positions and an electrophile is an electron-seeking species. All electron-donating groups behave similarly!
- the effect of the electron-withdrawing NO_2 group is to decrease electron density at the ortho and para positions of the ring. The electrophile reacts preferentially at the meta position since those are the most electron-rich positions. Most electron-withdrawing groups behave similarly!

<u>ELECTRON–DONATING GROUPS</u>

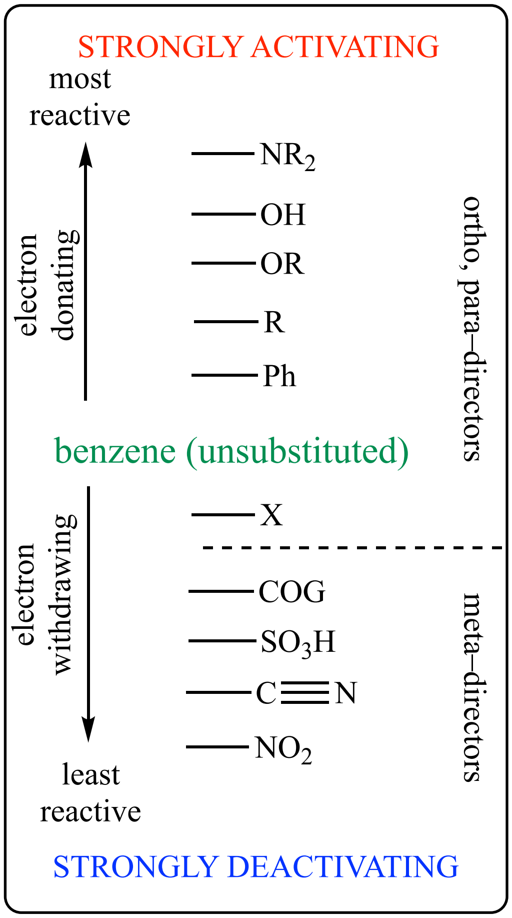


- most electron-donating groups have a lone pair on the atom attached to the benzene ring
- the lone pair pushes electron density into the ring via resonance interactions, increasing electron density

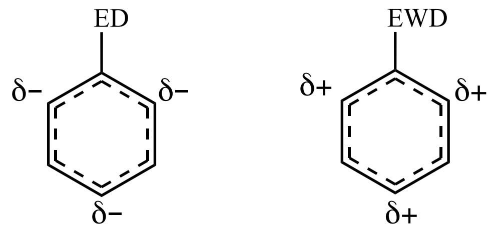
<u>ELECTRON–WITHDRAWING GROUPS</u>



- most electron-withdrawing groups have a positively charged, or partially-positively charged atom attached to the benzene
- the charge acts to pull electron density out of the benzene ring, depleting electron density



- the stronger the electron-donating ability of the substituent, the greater the amount of electron density in the ring
- the greater the amount of electron density in the ring the faster reaction with electrophiles and the more activating the substituent
- the stronger the electron-withdrawing ability of the substituent, the less amount of electron density in the ring
- the less the electron density in the ring, the slower the reaction with electrophiles and the more deactivating the substituent



ED = electron-donating substituent   EWD = electron-withdrawing substituent

- electron donating substituents will build up charge at the ortho and para positions
- electron donating substituents are termed "ortho, para-directors" since they direct reactivity to those positions
- electron withdrawing substituents deplete charge at the ortho and para positions
- electron withdrawing substituents are termed "meta" directors since they direct reactivity to that position
- an exception to the rule are the halogens, which are weakly deactivating (electron-withdrawing) but are ortho,para-directors

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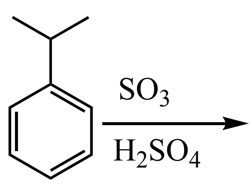
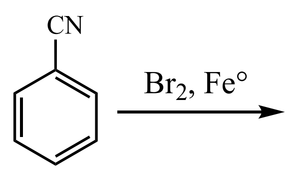
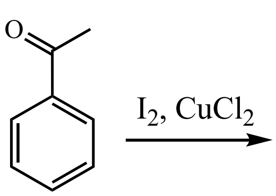
For the following, predict whether the reaction will be faster or slower than the corresponding reaction with benzene, and predict the major product(s)



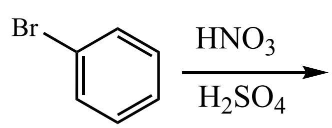
A



B



C

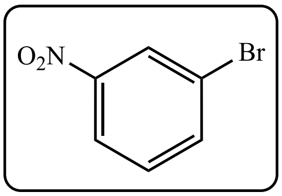


D

If all four of the aromatic compounds A-D were subjected to Br_2, $AlBr_3$ under otherwise identical conditions, what would be the order of reactivity from fastest to slowest?

Planning the Synthesis of an Aromatic Compound

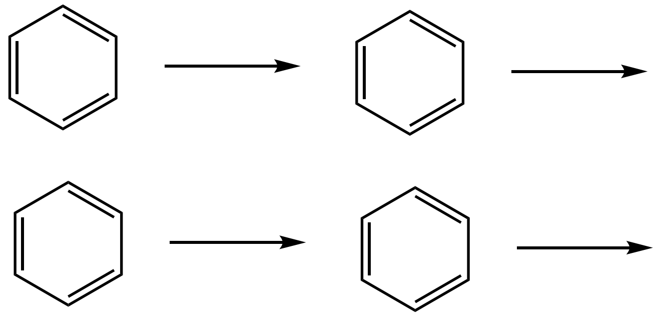
Plan a synthesis for each of the boxed aromatic compounds

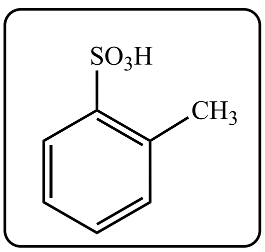


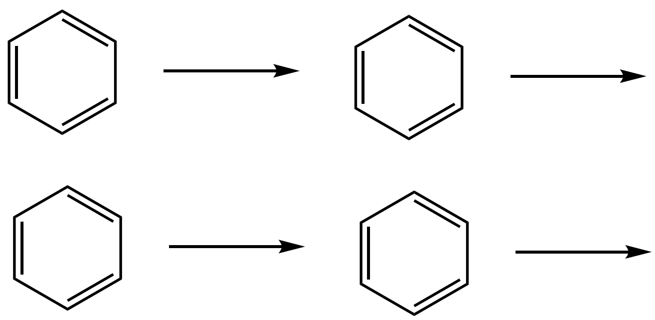
brominate first

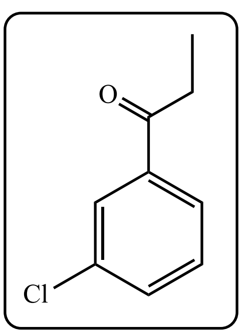
or

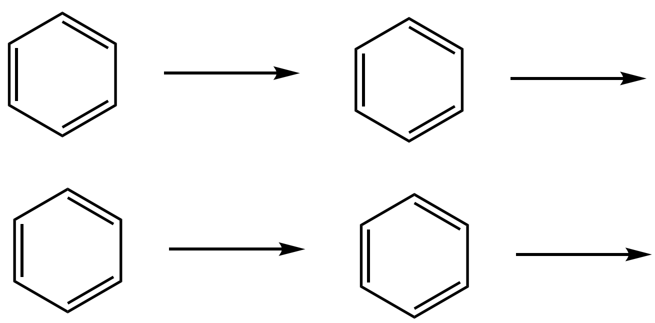
nitrate first







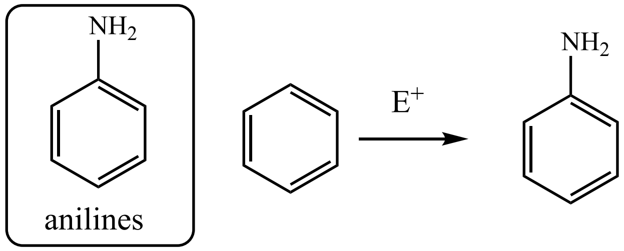




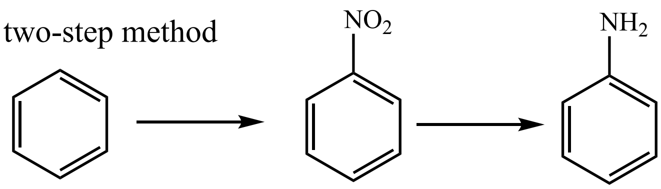
- the order in which reagents are added is often critical to obtaining the desired product!
- if the disubstituted product is meta substituted, put an electron-withdrawing substituent on first
- if both substituents are electron-withdrawing, from a practical standpoint, put the less deactivating group on first (if the MORE deactivating group is put on first, the second reaction will be VERY SLOW)
- if the disubstituted product is ortho or para substituted, put an electron donating substituent on first
- if both substituents are electron-donating, from a practical standpoint, put the more activating group on first (if the MORE activating group is put on first, the second reaction will be FASTER)

Problems: 3–7

How to Make Two Important Benzene Derivatives

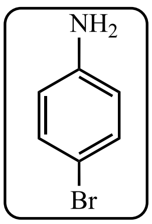


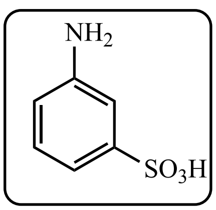
two-step method

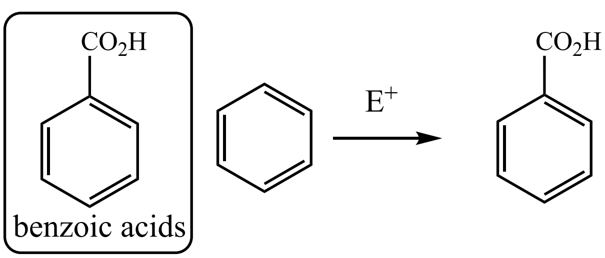


- there is no electrophile available to attach the NH_2 substituent in a single step
- the NH_2 substituent can be formed by using the NO_2 electrophile since this attaches a N atom to the ring
- reduction of the NO_2 substituent takes place using Fe°, Zn° or Sn° metal in HCl
- reduction of the NO_2 substituent to the NH_2 substituent forms the desired anilines via a two-step process
- NOTE that the NO_2 substituent is a powerful electron withdrawing substituent (meta director) while the NH_2 substituent is a powerful electron donating substituent (ortho,para director)

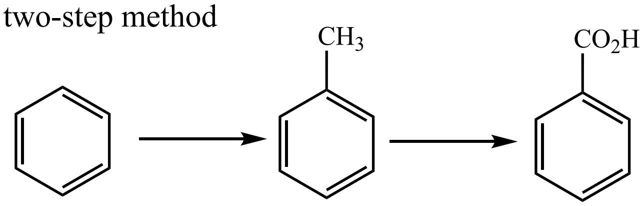
Plan a synthesis for each of the boxed aromatic compounds





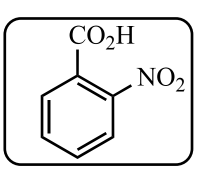


two-step method



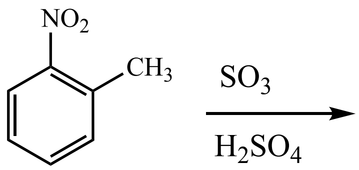
- there is no electrophile available to attach the CO_2H substituent in a single step
- the CO_2H substituent can be formed by using the Friedel-Crafts alkylation reaction since this attaches a C atom to the ring
- oxidation of the alkyl substituent (usually a methyl group) to the CO_2H substituent forms the desired carboxylic acids via a two-step process
- typically, $KMnO_4$ or the Jones reagent ($Na_2Cr_2O_7$, H_2SO_4, H_2O) are used for the reaction
- NOTE that the CO_2H substituent is an electron withdrawing substituent (meta director) while the alkyl substituent is a mild electron donating substituent (ortho,para director)

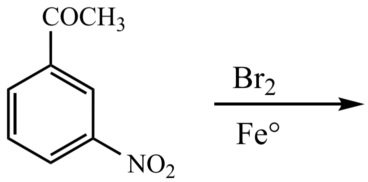
Plan a synthesis for the boxed aromatic compound



Problems: 8

EAS on Benzene Rings with Two (or more) Aromatic Substituents





• if the two substituent directing effects reinforce each other, the electrophile goes to the mutually beneficial site

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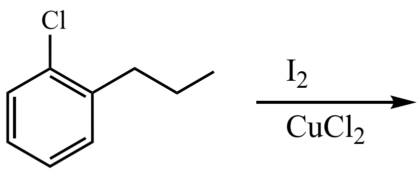

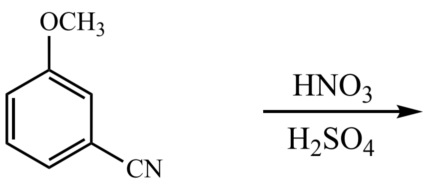

• if the directing effects of the two groups are conflicting, the stronger electron donating group prevails
• electrophiles avoid reacting at the position between two other substituents due to large steric strain energy that would result

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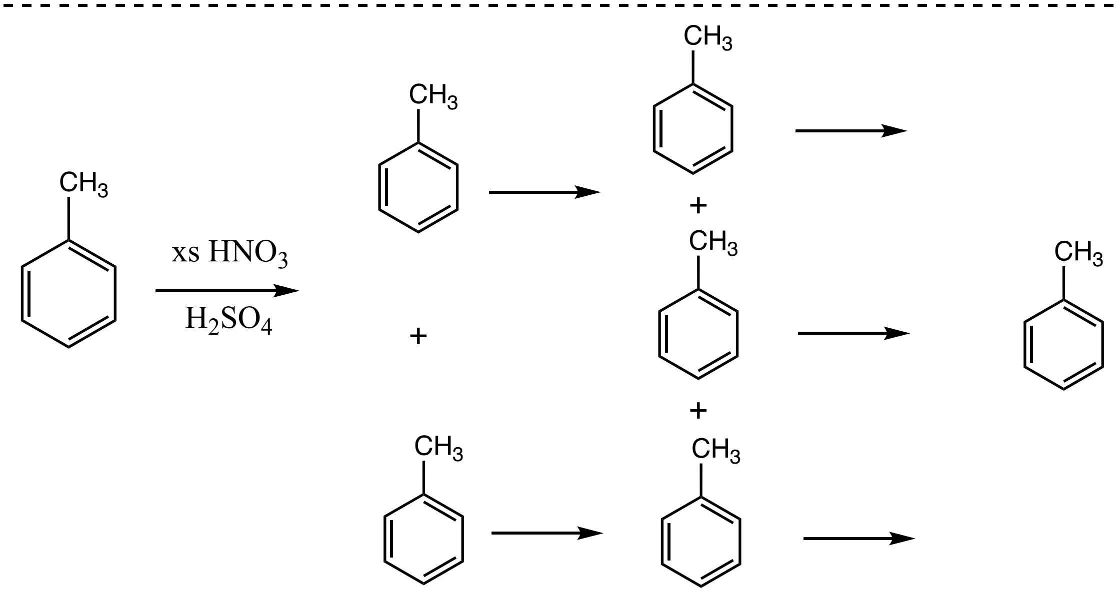
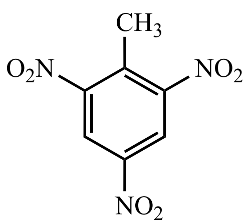
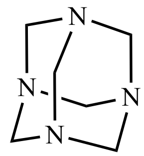


Problems: 9, 10

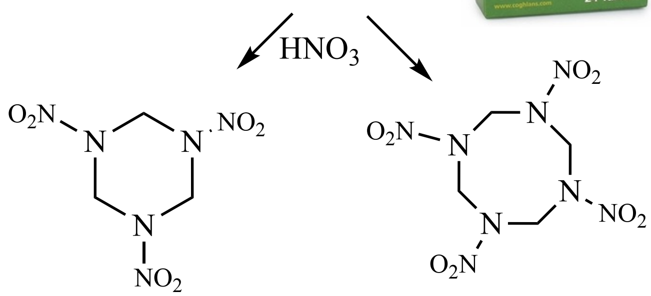
Some Common Explosives (boom!)



trinitrotoluene
(TNT)

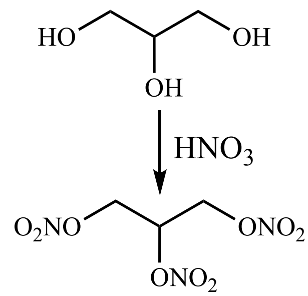


hexamine



RDX
"plastic" explosive

HMX
nuclear arms detonator
rocket propellant

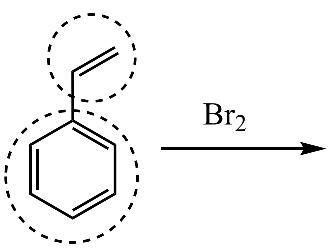


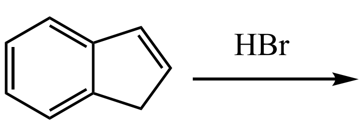
nitroglycerine

Alfred Nobel
1833-1896

CxHyNzOw ⟶ $CO_2 + H_2O + N_2 +$

Reactivity of Compounds Containg Benzene Rings AND C=C Bonds





• remember that a benzylic carbocation is particularly stable due to resonance interactions with the aromatic ring.
• therefore, a benzylic carbocation will be formed preferentially to an ordinary alkyl carbocation