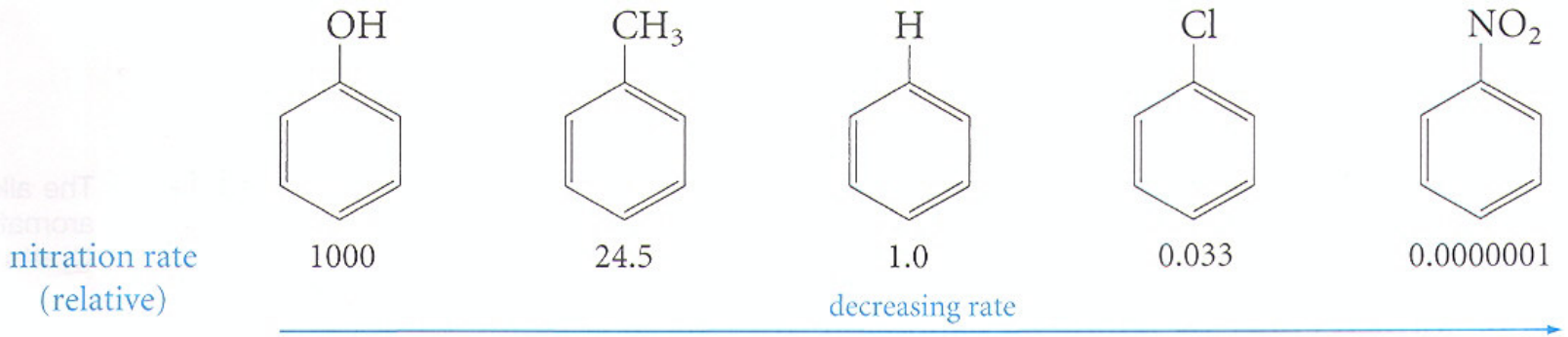
4.10 Ring-Activating and Ring-Deactivating Substituents

In this section and the next, we will present experimental evidence that supports the electrophilic aromatic substitution mechanism just described. We will do this by examining how substituents already present on an aromatic ring affect further substitution reactions.

For example, consider the relative nitration rates of the following compounds, all under the same reaction conditions:

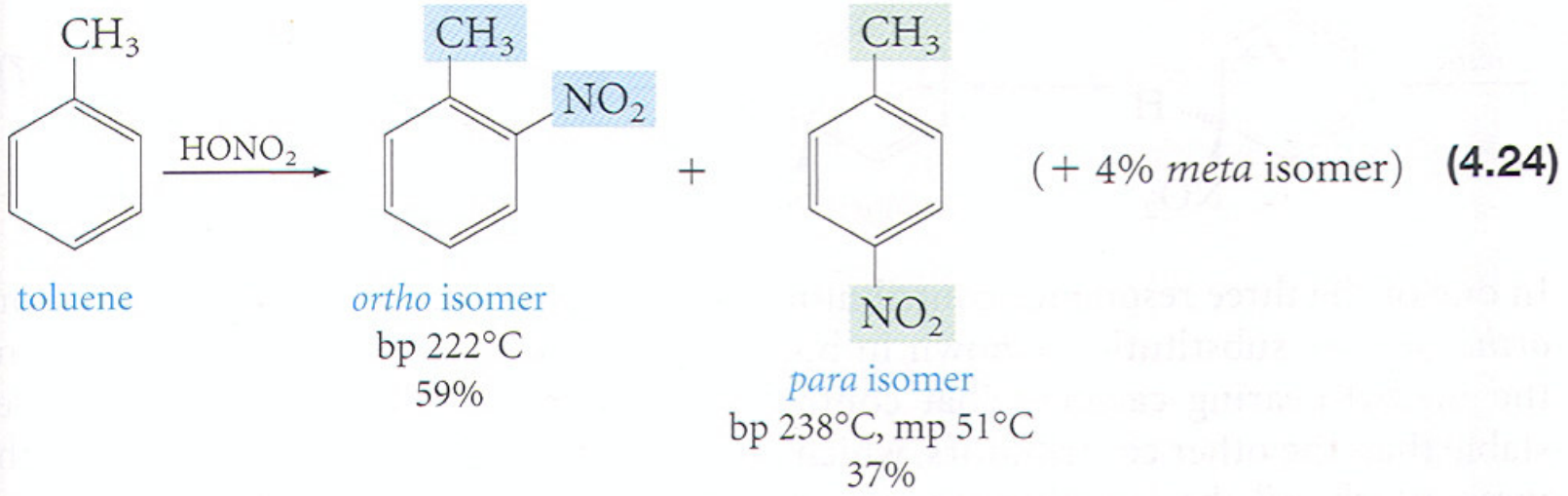


Effects of Substituents on Reactivity and Orientation

- The nature of groups already on an aromatic ring affect both the reactivity and orientation of future substitution
  - Activating groups cause the aromatic ring to be more reactive than benzene
  - Deactivating groups cause the aromatic ring to be less reactive than benzene
  - Ortho-para directors direct future substitution to the ortho and para positions
  - Meta directors direct future substitution to the meta position

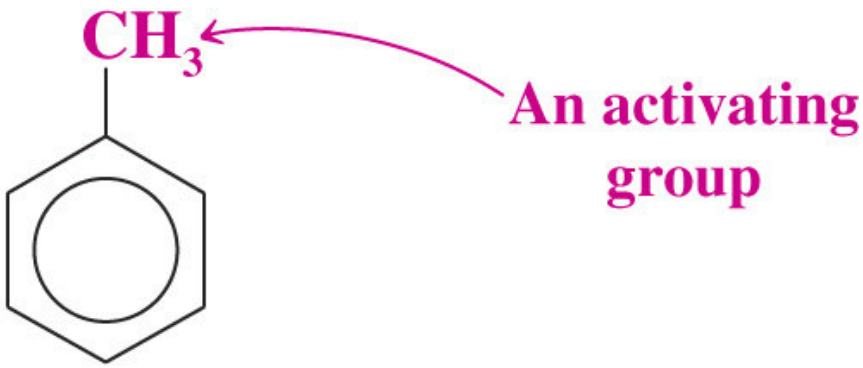
4.11 *Ortho,Para*-Directing and *Meta*-Directing Groups

Substituents already present on an aromatic ring determine the position taken by a new substituent. For example, nitration of toluene gives mainly a mixture of *o*- and *p*-nitrotoluene.



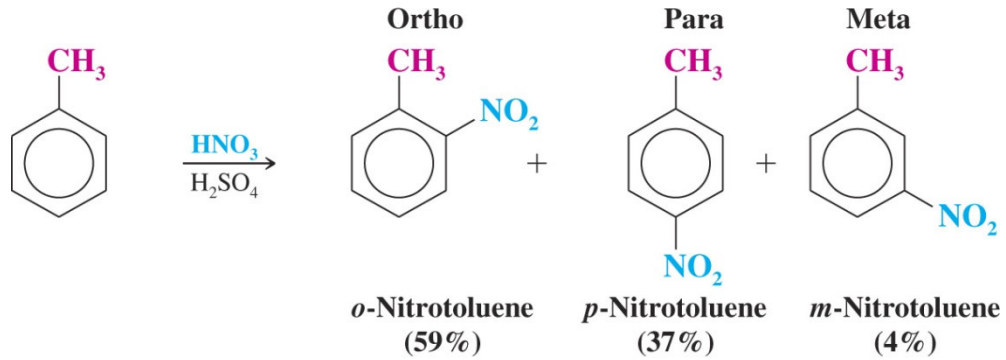
4.11.a Activating Groups: Ortho-Para Directors

- All activating groups are also ortho-para directors
  - The halides are also ortho-para directors but are mildly deactivating
- The methyl group of toluene is an ortho-para director
  - Toluene reacts more readily than benzene, *e.g.* at a lower temperatures than benzene

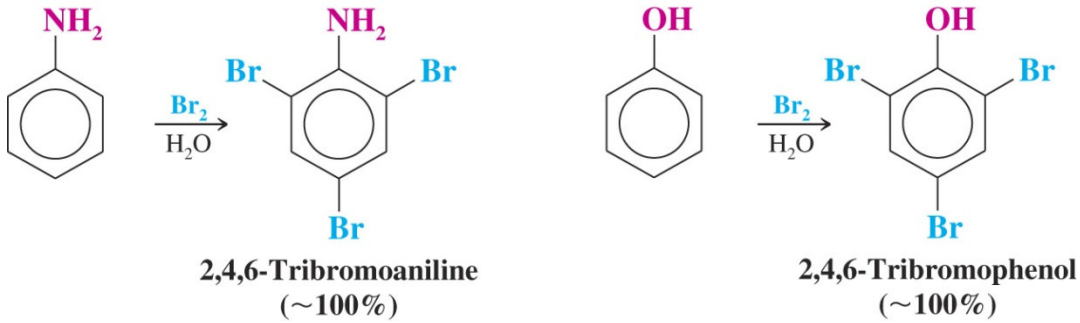


More reactive than benzene toward electrophilic substitution

- The methyl group of toluene is an ortho-para director

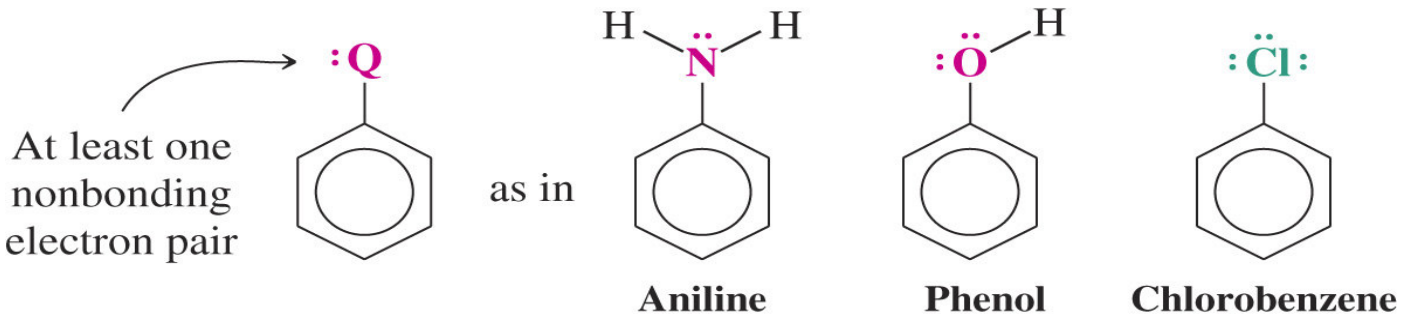


- Amino and hydroxyl groups are also activating and ortho-para directors
  - These groups are so activating that catalysts are often not necessary

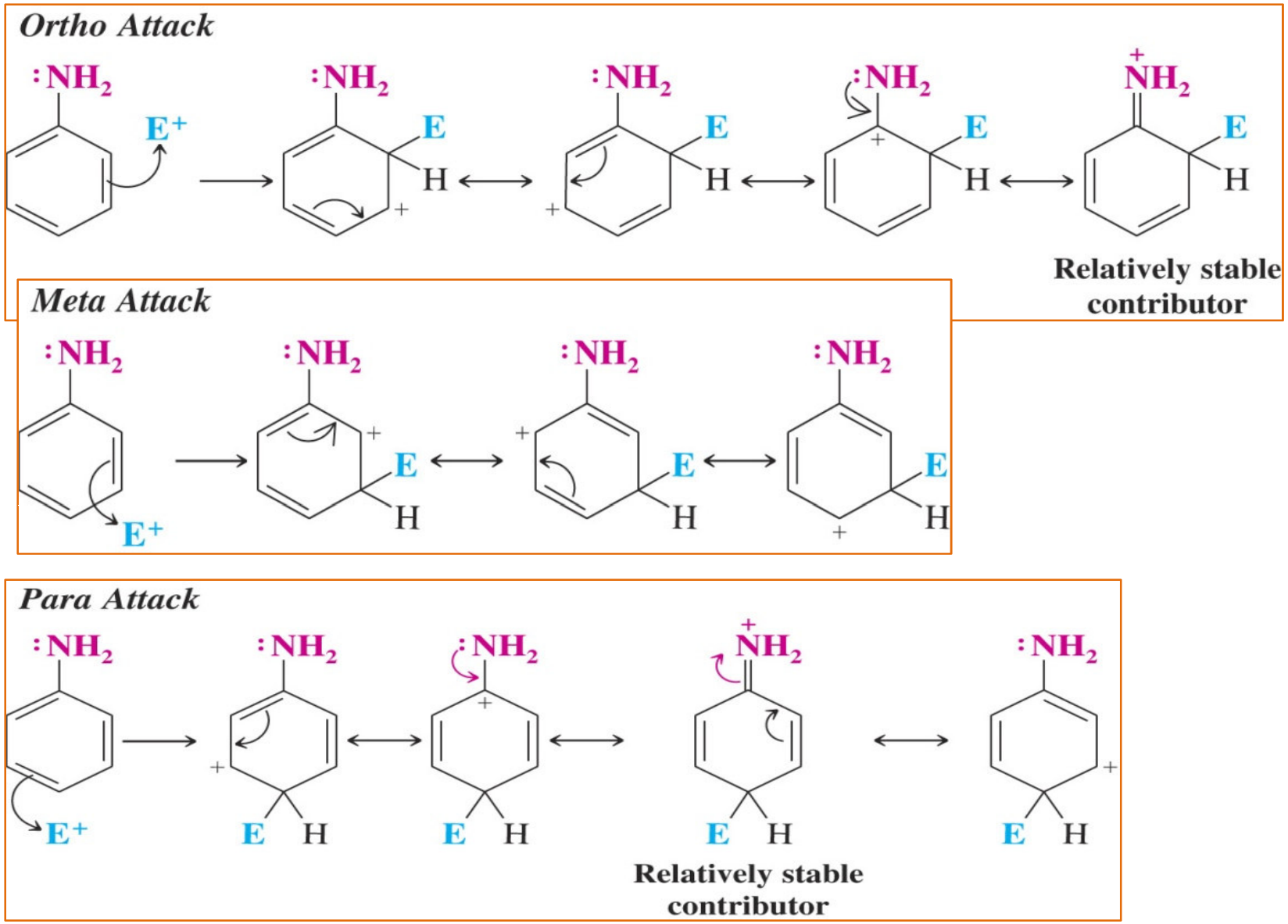


- Alkyl groups and heteroatoms with one or more unshared electron pairs directly bonded to the aromatic ring will be ortho-para directors.

- Many ortho-para directors are groups that have a lone pair of electrons on the atom directly attached to the ring



- Activating groups having unshared electrons on the atom bonded to the ring exert primarily a resonance effect
  - The aromatic ring is activated because of the resonance effect of these groups
  - They are ortho-para directors because they contribute a fourth important resonance form which stabilizes the arenium ion in the cases of ortho and para substitution only
  - The fourth resonance form that involves the heteroatom is particularly important because the octet rule is satisfied for all atoms in the arenium ion


Ortho Attack
:NH2
E+
E
H
Relatively stable contributor
Meta Attack
Para Attack

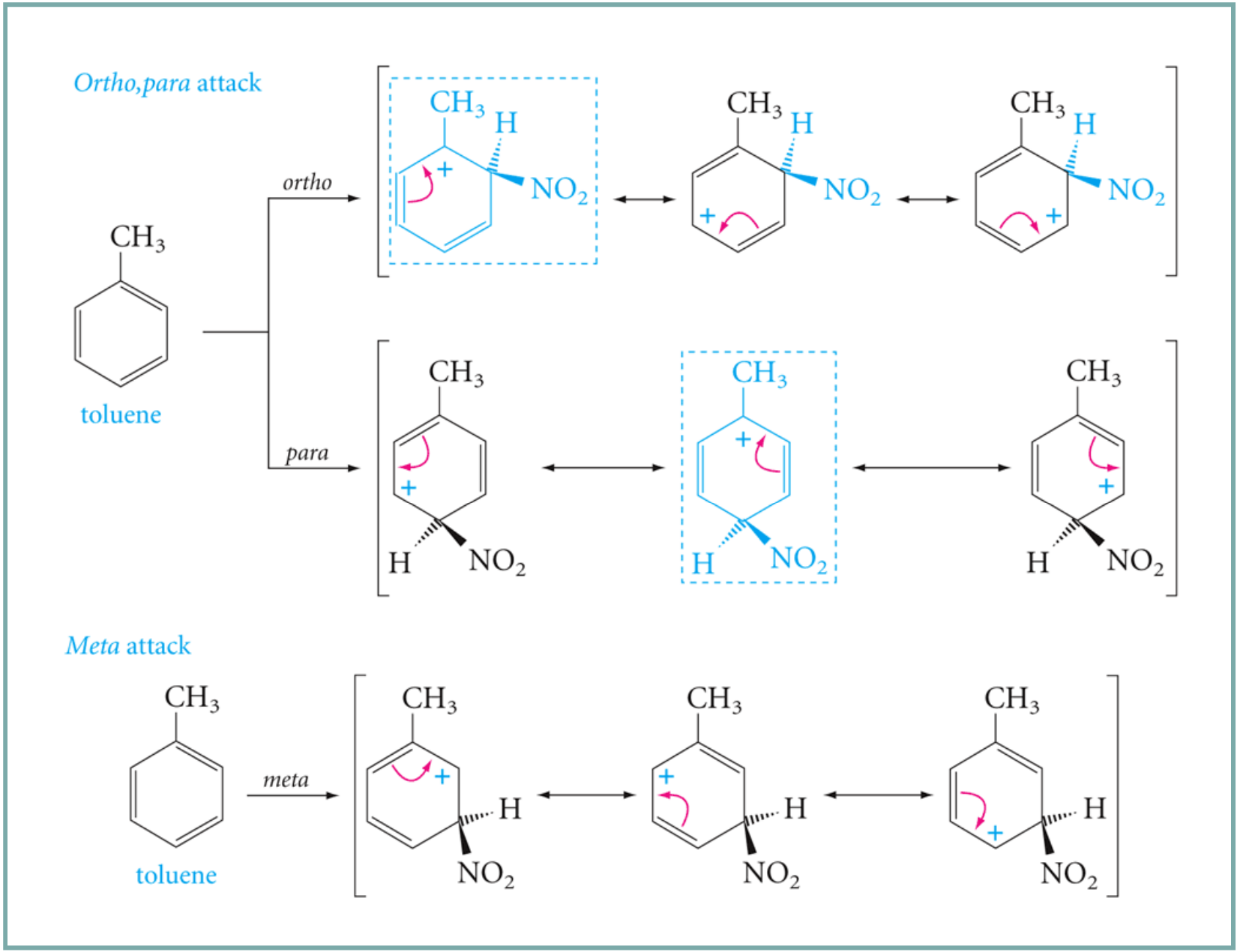
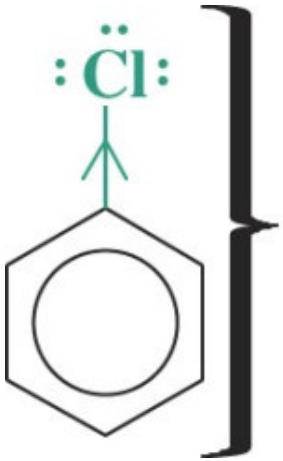

Ortho,para attack
ortho
para
toluene
Meta attack
meta
toluene

Table 4.1 Directing and activating effects of common functional groups (groups are listed in decreasing order of activation)

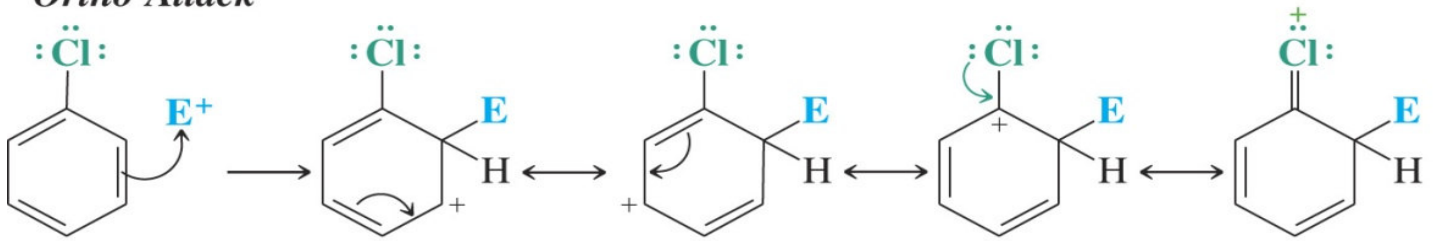
	Substituent group	Name of group	
Ortho,Para-Directing	$-\ddot{N}H_2$, $-\ddot{N}HR$, $-\ddot{N}R_2$	amino	Activating
	$-\ddot{O}H$, $-\ddot{O}CH_3$, $-\ddot{O}R$	hydroxy, alkoxy	
	$-\ddot{N}HC(=O)-R$	acylamino	
	$-CH_3$, $-CH_2CH_3$, $-R$	alkyl	
	$-\ddot{F}:$, $-\ddot{Cl}:$, $-\ddot{Br}:$, $-\ddot{I}:$	halo	Deactivating
Meta-Directing	$-C(=O)-R$ $\quad$ $-C(=O)-\ddot{O}H$	acyl, carboxy	
	$-C(=O)-\ddot{N}H_2$ $\quad$ $-C(=O)-\ddot{O}R$	carboxamido, carboalkoxy	
	$-S(=O)(=O)-\ddot{O}H$	sulfonic acid	
	$-C\equiv N:$	cyano	
	$-N^{+}(=O:)-\ddot{O}:^{-}$	nitro	

- Halo groups are ortho-para directors but are also deactivating
  - The electron-withdrawing inductive effect of the halide is the primary influence that deactivates haloaromatic compounds toward electrophilic aromatic substitution
  - The electron-donating resonance effect of the halogen's unshared electron pairs is the primary ortho-para directing influence



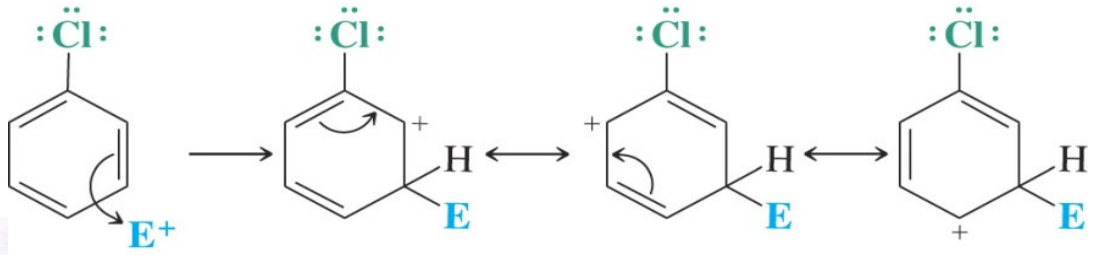
Inductive effect of chlorine atom deactivates ring.

Ortho Attack

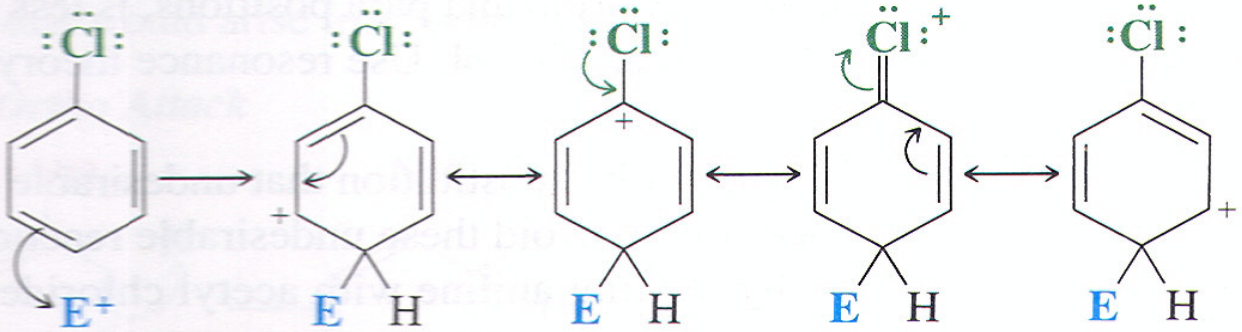


Relatively stable contributor

Meta attack



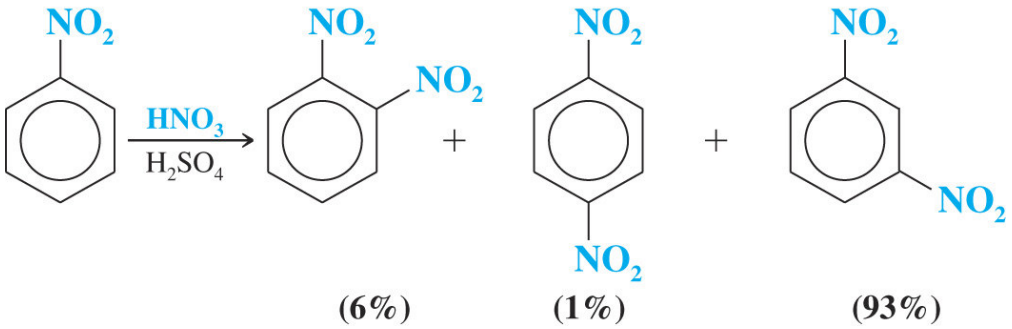
Para Attack



Relatively stable contributor

4.11.b Deactivating Groups: Meta Directors

- Strong electron-withdrawing groups such as nitro, carboxyl, and sulfonate are deactivators and meta directors



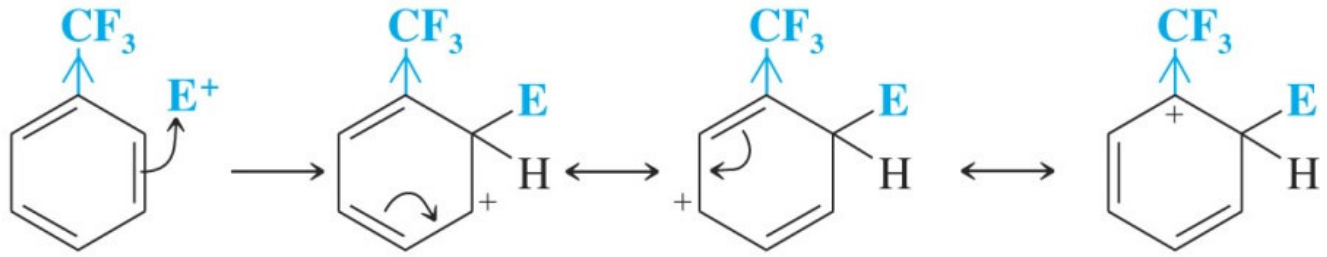
– Halo Substitutents: Deactivating Ortho-Para Directors

- Chloro and bromo groups are weakly deactivating but are also ortho, para directors
  – In electrophilic substitution of chlorobenzene, the ortho and para products are major:

Reaction	Ortho Product (%)	Para Product (%)	Total Ortho and Para (%)	Meta Product (%)
Chlorination	39	55	94	6
Bromination	11	87	98	2
Nitration	30	70	100	
Sulfonation		100	100	

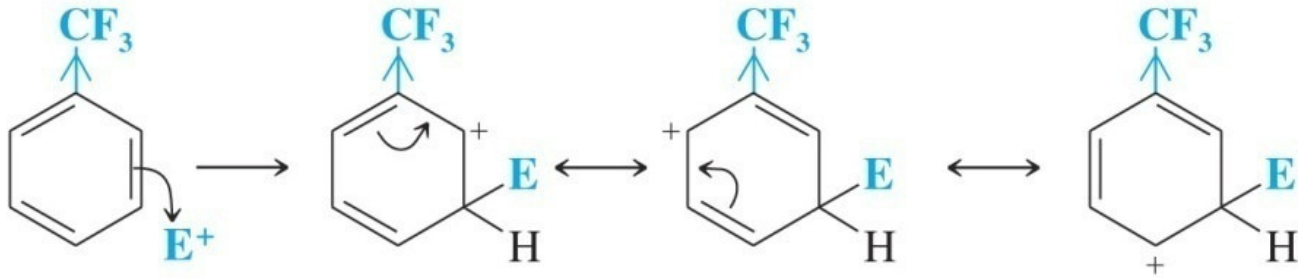
- Meta-directing Groups
  - All meta-directing groups have either a partial or full positive charge on the atom directly attached to the aromatic ring
  - The trifluoromethyl group destabilizes the arenium ion intermediate in ortho and para substitution pathways
    - The arenium ion resulting from meta substitution is not so destabilized and therefore meta substitution is favored

Ortho Attack

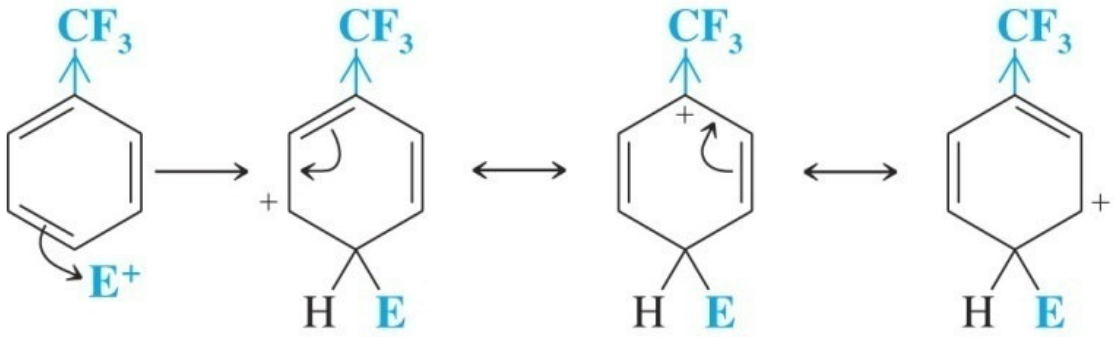


Highly unstable contributor

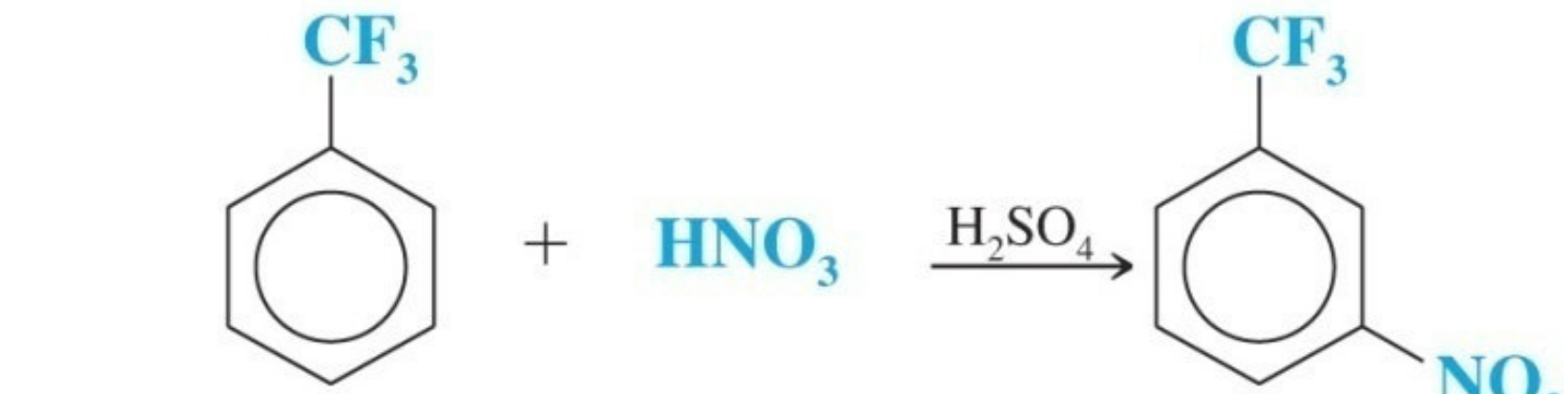
Meta Attack



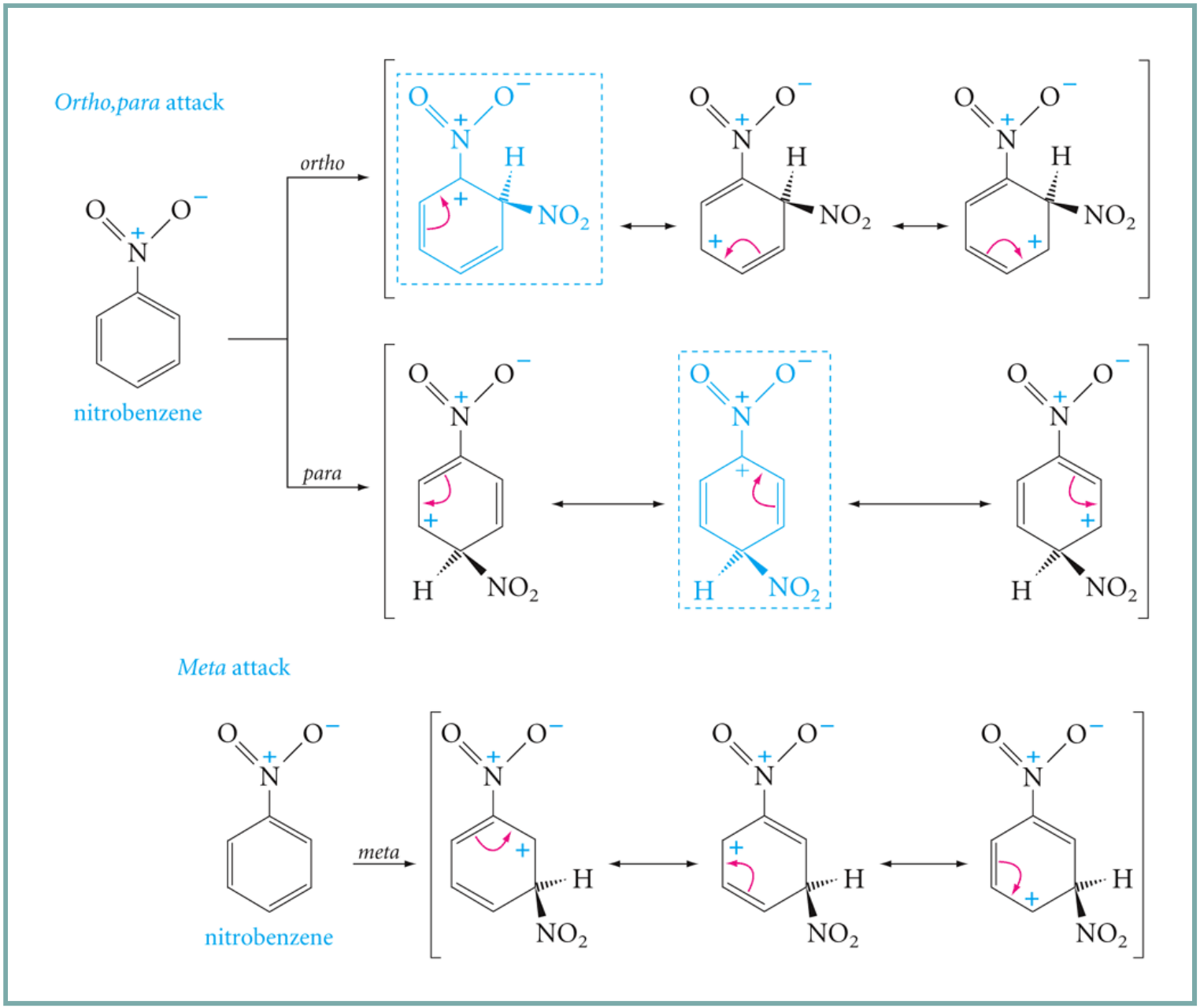
Para Attack



Highly unstable contributor



Trifluoromethylbenzene **(~100%)**

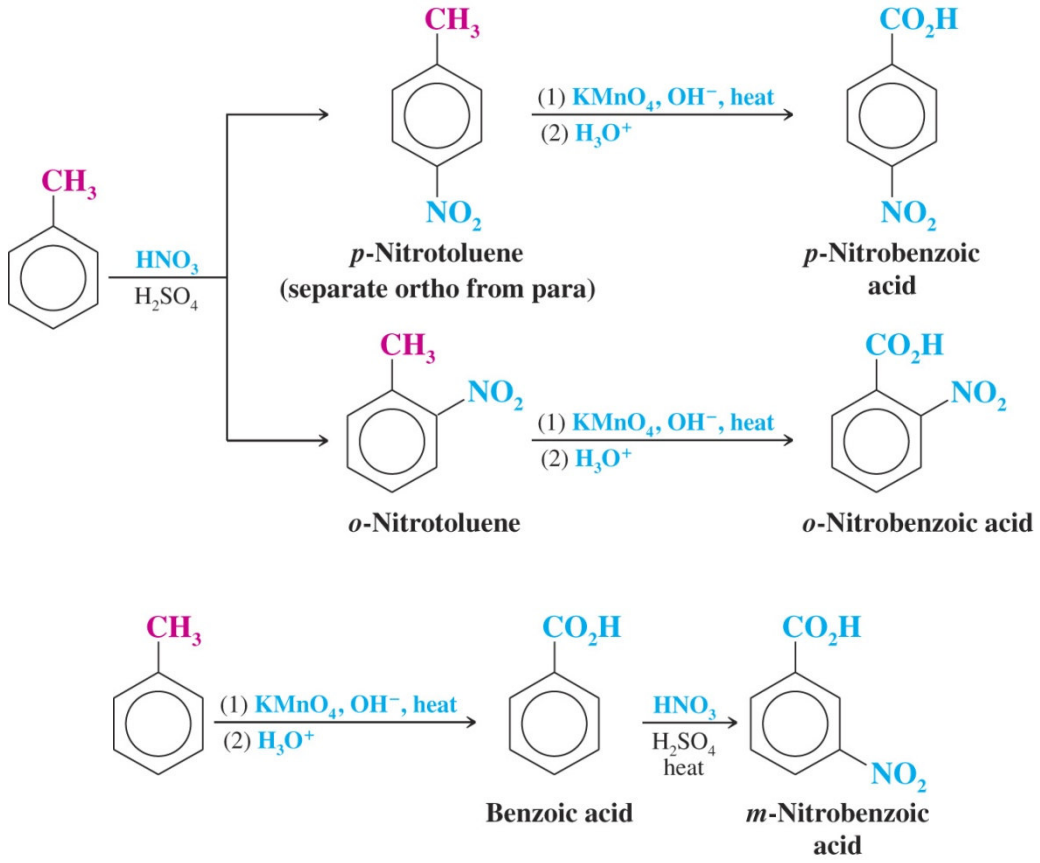

Ortho,para attack
ortho
para
nitrobenzene
Meta attack
meta
nitrobenzene

4.11.c Substitution Effects on Reactivity

Ortho–Para Directors	Meta Directors
Strongly Activating —$\ddot{N}H_2$, —$\ddot{N}HR$, —$\ddot{N}R_2$ —$\ddot{O}H$, —$\ddot{O}:^-$	**Moderately Deactivating** —C≡N —SO_3H —CO_2H, —CO_2R —CHO, —COR
Moderately Activating —$\ddot{N}HCOCH_3$, —$\ddot{N}HCOR$ —$\ddot{O}CH_3$, —$\ddot{O}R$	**Strongly Deactivating** —NO_2 —NR_3^+ —CF_3, —CCl_3
Weakly Activating —CH_3, —C_2H_5, —R —C_6H_5	
Weakly Deactivating —$\ddot{F}:$, —$\ddot{C}l:$, —$\ddot{B}r:$, —$\ddot{I}:$	

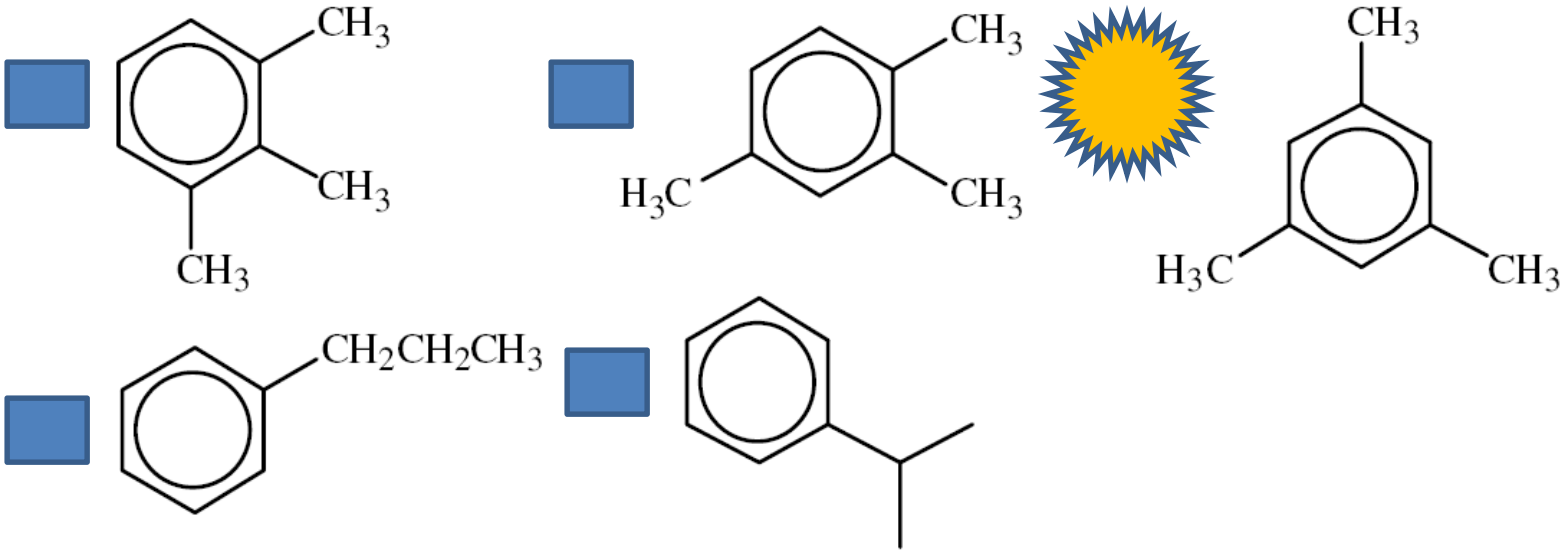
4.12 the Importance of Directing Effects in Synthesis

- When designing a synthesis of substituted benzenes, the order in which the substituents are introduced is crucial
- Example: Synthesize ortho-, meta-, and para-nitrobenzoic acid from toluene



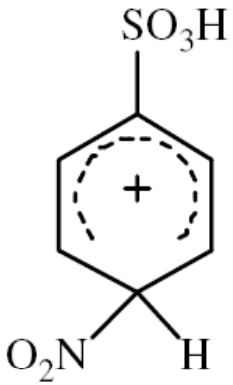
Selected Examples

Which alkylbenzene, C_9H_{12}, when nitrated can yield only one mononitro product?

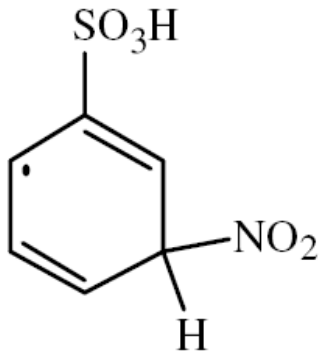


The predominant intermediate in the nitration of benzenesulfonic acid is

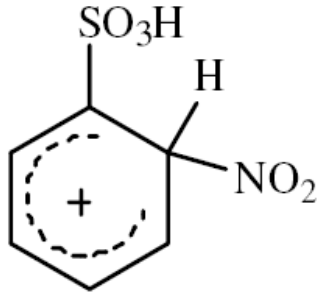
a.



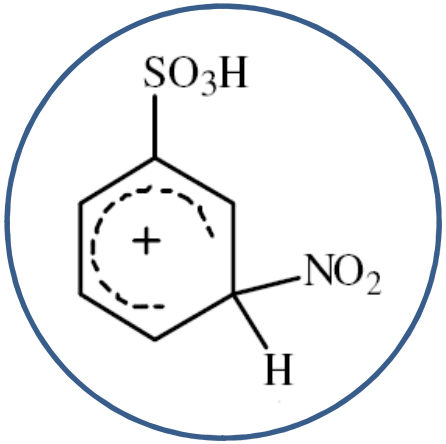
b.



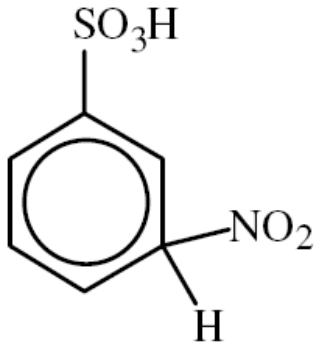
c.



d.



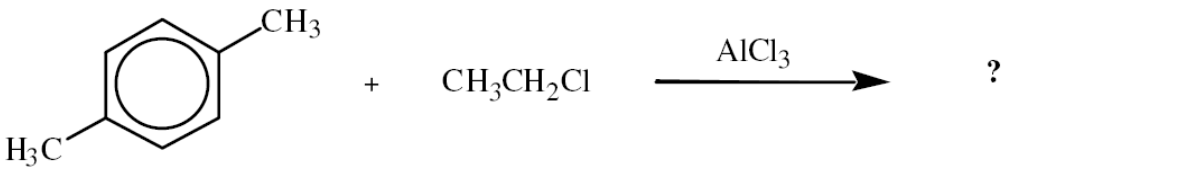
e.



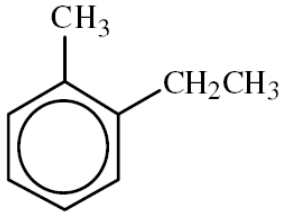
Which of the following groups is a *meta* director?

a. –Cl **b.** –CHO **c.** $-OCH_3$ **d.** –OH **e.** –Ar

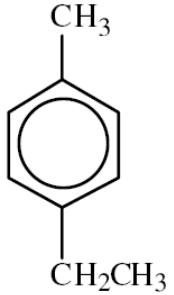
The expected product from the following reaction is:



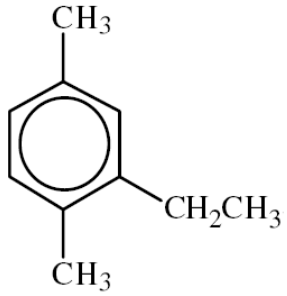
a.



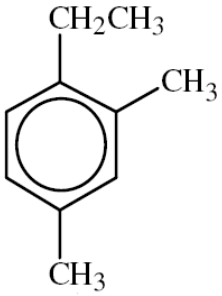
b.



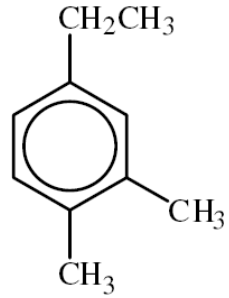
***c.**



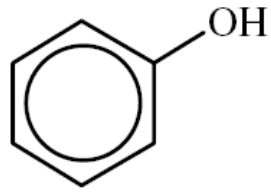
d.



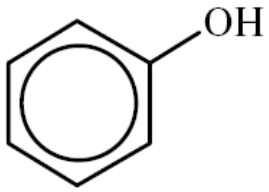
e.



What is the best sequence of reactions to synthesize *m*-nitrophenol?

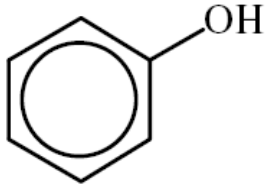
a. 

$\xrightarrow[H_2SO_4]{HNO_3}$

b. 

$\xrightarrow[2)\ H_2O,\ \Delta]{1)\ HNO_3,\ H_2SO_4}$

c. 
$\xrightarrow[2)\ NaOH,\ 200^oC\\ 3)\ HNO_3,\ H_2SO_4]{1)\ H_2SO_4,\ \Delta}$

d. 

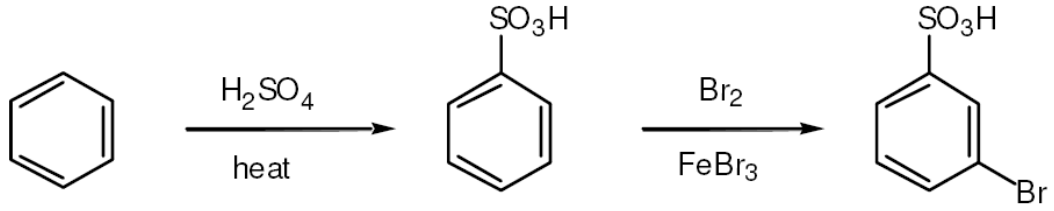
$\xrightarrow[2)\ NaOH,\ 200^oC]{1)\ H_2SO_4,\ \Delta}$

e. 
$\xrightarrow[2)\ H_2SO_4,\ \Delta\\ 3)\ NaOH,\ 200^oC]{1)\ HNO_3,\ H_2SO_4}$

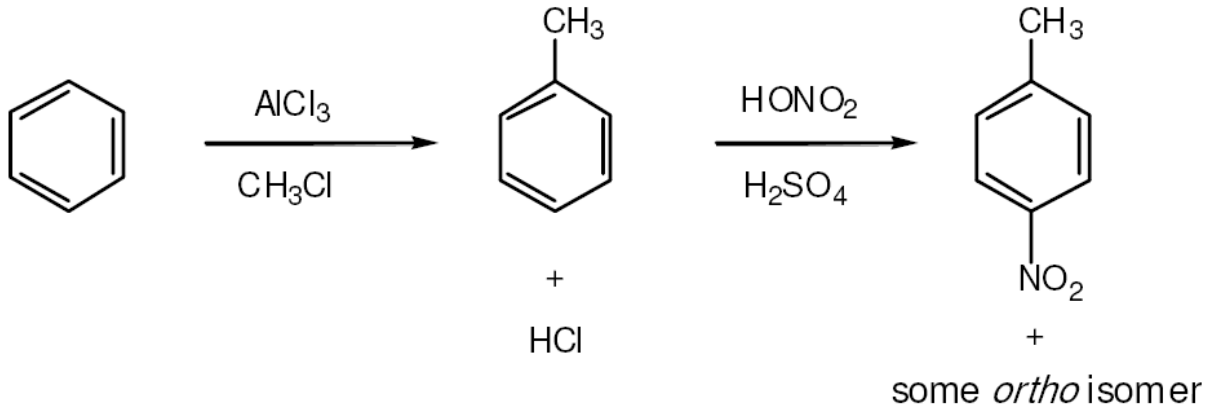
PROBLEM 4.16 Devise a synthesis for each of the following, starting with benzene:

a. *m*-bromobenzenesulfonic acid
b. *p*-nitrotoluene

4.16 a. Since the substituents are *meta* in the product, we must introduce the *meta*-directing substituent first:



b. The methyl substituent is *ortho,para*-directing; the two isomers obtained in the final step would have to be separated. Usually the *para* isomer, in which the two substituents are furthest apart, predominates.

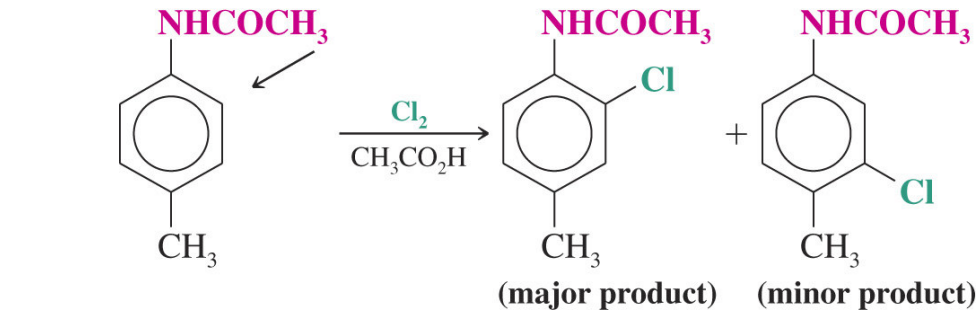


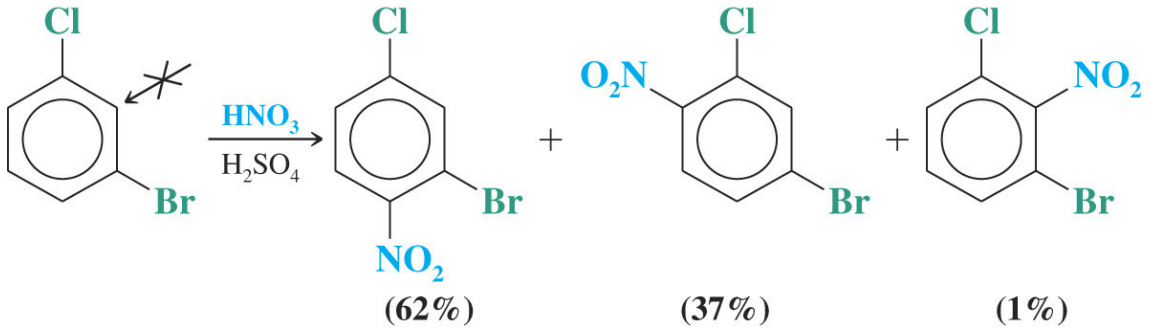
PROBLEM 4.17 Explain why it is *not* possible to prepare *m*-bromochlorobenzene or *p*-nitrobenzenesulfonic acid by carrying out two successive electrophilic aromatic substitutions.

4.17 We could not make *m*-bromochlorobenzene in good yield this way because both Br and Cl are *ortho,para*-directing. Similarly, we could not prepare *p*-nitrobenzenesulfonic acid directly because both the nitro and sulfonic acid substituents are *meta*-directing.

– Orientation in Disubstituted Benzenes

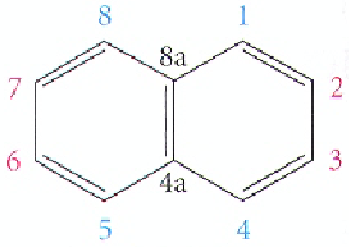
- When two substituents are present on the ring initially, the more powerful activating group generally determines the orientation of subsequent substitution
  - Ortho-para directors determine orientation over meta directors
  - Substitution does not occur between meta substituents due to steric hindrance



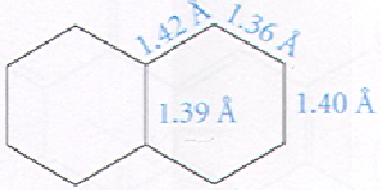


4.13 Polycyclic Aromatic Hydrocarbons

The concept of **aromaticity**—the unusual stability of certain fully conjugated **cyclic** systems—can be extended well beyond benzene itself or simple substituted benzenes.*



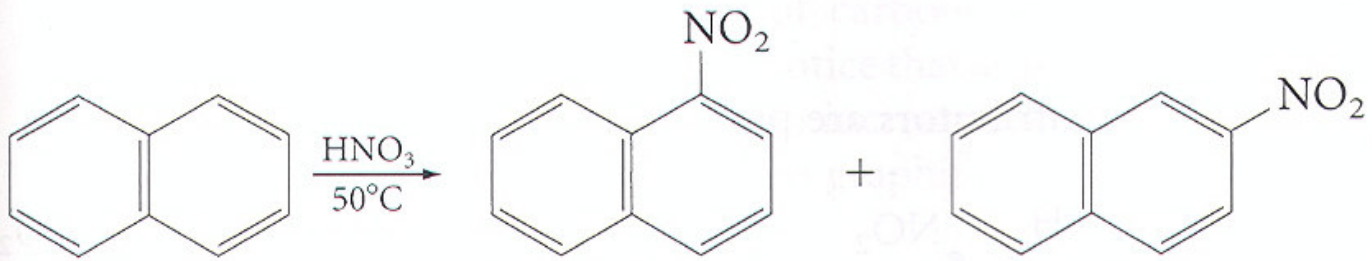
naphthalene
mp 80°C



bond lengths in naphthalene

The bond lengths in naphthalene are not all identical, but they all approximate the bond length in benzene (1.39 Å). Although it has two six-membered rings, naphthalene has a resonance energy somewhat less than twice that of benzene, about 60 kcal/mol. Because of its symmetry, naphthalene has three sets of equivalent carbon atoms: C-4a and C-8a; C-1, C-4, C-5, and C-8; and C-2, C-3, C-6, and C-7. Like benzene, naphthalene undergoes electrophilic substitution reactions (halogenation, nitration, and so on), usually under somewhat milder conditions than benzene. Although two monosubstitution products are possible, substitution at C-1 usually predominates.

Like benzene, naphthalene undergoes electrophilic substitution reactions (halogenation, nitration, and so on), usually under somewhat milder conditions than benzene. Although two monosubstitution products are possible, substitution at C-1 usually predominates.



(4.34)

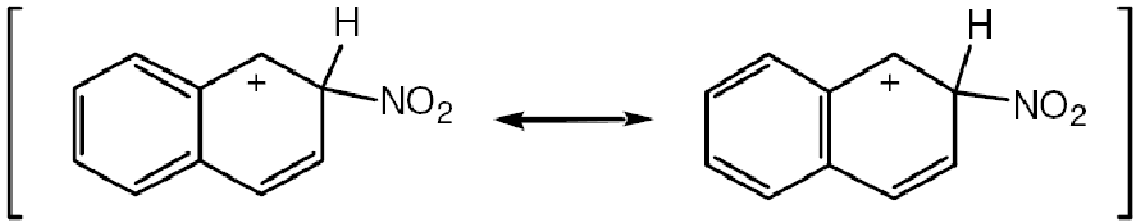
1-nitronaphthalene (ratio 10:1) 2-nitronaphthalene

EXAMPLE 4.3

Draw the resonance contributors for the carbocation intermediate in nitration of naphthalene at C-1; include only structures that retain benzenoid aromaticity in the unsubstituted ring.

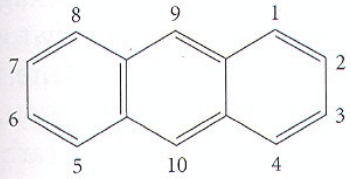
PROBLEM 4.18 Repeat Example 4.3 for nitration at C-2. Can you suggest why substitution at C-1 is preferred?

4.18 Only two such contributors are possible:

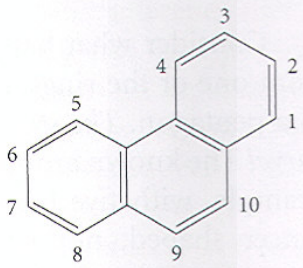


Any additional resonance contributors disrupt the benzenoid structure in the "left" ring. Since the intermediate carbocation for nitration of naphthalene at C-1 is more stable, substitution at that position is preferred.

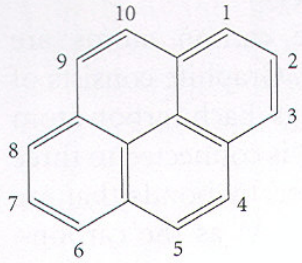
Naphthalene is the parent compound of a series of **fused polycyclic hydrocarbons**, a few other examples of which are



anthracene
mp 217°C



phenanthrene
mp 98°C



pyrene
mp 156°C

Infinite extension of such rings leads to sheets of hexagonally arranged carbons, the structure of graphite (a form of elemental carbon).

Fused polycyclic hydrocarbons contain at least two benzene rings; each ring shares two carbon atoms with at least one other ring.

Dr. Abdullah I. Saleh

End of Chapter 4