Rate and Regioselectivity in Electrophilic Aromatic Substitution

A substituent already present on the ring affects both the rate and regioselectivity of electrophilic aromatic substitution.

Effect on Rate

Activating substituents increase the rate compared to that of benzene.

Deactivating substituents decrease the rate compared to benzene.

Methyl Group

Toluene undergoes nitration 20-25 times faster than benzene.

A methyl group is an activating substituent.

Trifluoromethyl Group

(Trifluoromethyl)benzene undergoes nitration 40,000 times more slowly than benzene .

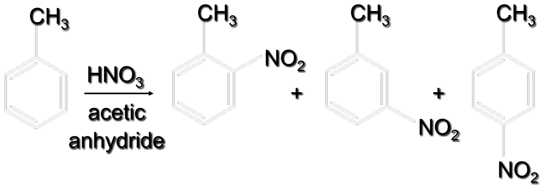
A trifluoromethyl group is a deactivating substituent.

Effect on Regioselectivity

Ortho-para directors direct an incoming electrophile to positions ortho and/or para to themselves.

Meta directors direct an incoming electrophile to positions meta to themselves.

Nitration of Toluene



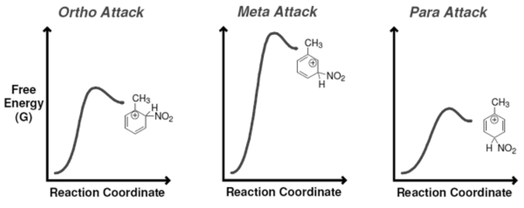
63% 3% 34%

o- and *p*-nitrotoluene together comprise 97% of the product

a methyl group is an ortho-para director

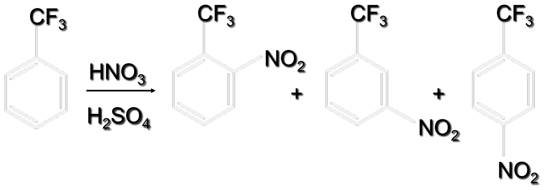
Nitration of Toluene

The ortho product predominates due to statistical probability.



63% 3% 34%

Nitration of (Trifluoromethyl)benzene



6% 91% 3%

m-nitro(trifluoromethyl)benzene comprises 91% of the product

a trifluoromethyl group is a meta director

Substituent Effects in Electrophilic Aromatic Substitution: Activating Substituents

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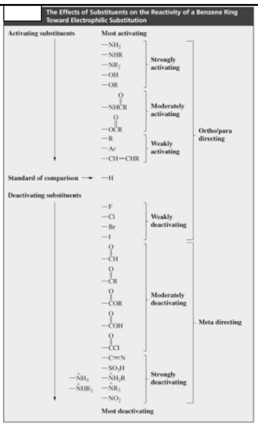
Table

Classification of Substituents in Electrophilic Aromatic Substitution Reactions

Very strongly activating
Strongly activating
Activating
Standard of comparison is H
Deactivating
Strongly deactivating
Very strongly deactivating



The Effects of Substituents on the Reactivity of a Benzene Ring Toward Electrophilic Substitution

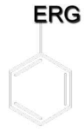
	Substituent	Reactivity	Directing
Activating substituents	**Most activating**		
	$-\mathrm{NH_2}$	**Strongly activating**	**Ortho/para directing**
	$-\mathrm{NHR}$		
	$-\mathrm{NR_2}$		
	$-\mathrm{OH}$		
	$-\mathrm{OR}$		
	$-\mathrm{NH}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{R}$	**Moderately activating**	
	$-\mathrm{O}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{R}$		
	$-\mathrm{R}$	**Weakly activating**	
	$-\mathrm{Ar}$		
	$-\mathrm{CH}{=}\mathrm{CHR}$		
Standard of comparison →	$-\mathrm{H}$		
Deactivating substituents			
	$-\mathrm{F}$	**Weakly deactivating**	
	$-\mathrm{Cl}$		
	$-\mathrm{Br}$		
	$-\mathrm{I}$		
	$-\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{H}$	**Moderately deactivating**	**Meta directing**
	$-\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{R}$		
	$-\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{OR}$		
	$-\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{OH}$		
	$-\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{Cl}$		
	$-\mathrm{C}{\equiv}\mathrm{N}$	**Strongly deactivating**	
	$-\mathrm{SO_3H}$		
$-\overset{+}{\mathrm{N}}\mathrm{H_3}$	$-\overset{+}{\mathrm{N}}\mathrm{H_2R}$		
$-\overset{+}{\mathrm{N}}\mathrm{HR_2}$	$-\overset{+}{\mathrm{N}}\mathrm{R_3}$		
	$-\mathrm{NO_2}$		
	Most deactivating		

Generalizations

1. All activating substituents are ortho-para directors.
2. Halogen substituents are slightly deactivating but ortho-para directing.
3. Strongly deactivating substituents are meta directors.

Electron-Releasing Groups (ERGs)

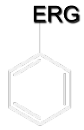
are ortho-para directing and activating



ERGs include —R, —Ar, and —C=C

Electron-Releasing Groups (ERGs)

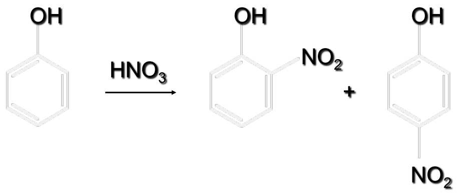
are ortho-para directing and strongly activating



ERGs such as —OH, and —OR are strongly activating

Nitration of Phenol

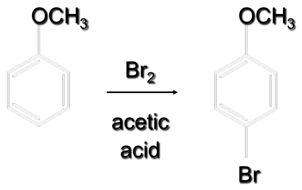
occurs about 1000 times faster than nitration of benzene



44% 56%

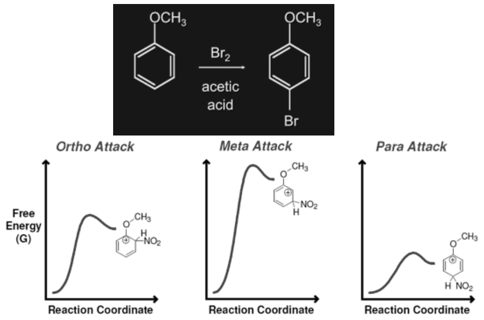
Bromination of Anisole

$FeBr_3$ catalyst is not necessary

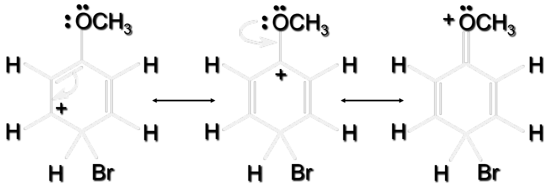


90%

Bromination of Anisole

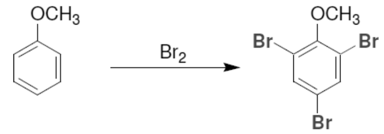


Oxygen Lone Pair Stabilizes Intermediate



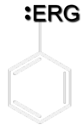
all atoms have octets

Methoxy is a Strong Activator



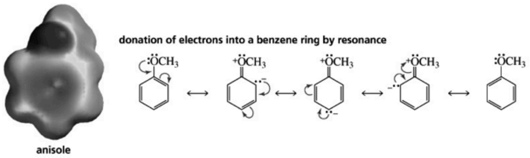
The methoxy group activates the ring so strongly that polysubstitution is difficult to avoid.

Electron-Releasing Groups (ERGs) or Electron "Donors"

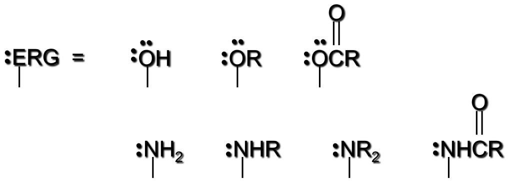


ERGs with a lone pair on the atom directly attached to the ring are ortho-para directing and strongly activating

A substituent can donate electrons into the ring by delocalizing its lone-pair electrons (resonance):

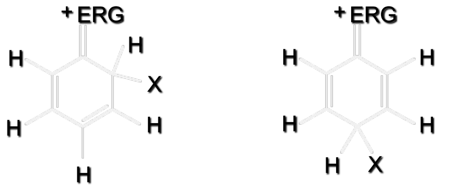


Examples



All of these are ortho-para directing and strongly to very strongly activating

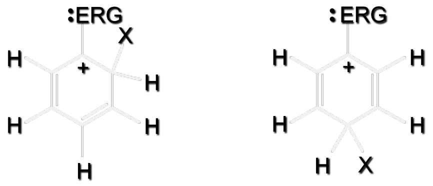
Lone Pair Stabilizes Intermediates for ortho and para Substitution



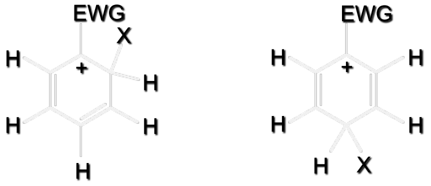
comparable stabilization not possible for intermediate leading to meta substitution

Substituent Effects in Electrophilic Aromatic Substitution: Strongly Deactivating Substituents

ERGs Stabilize Intermediates for ortho and para Substitution



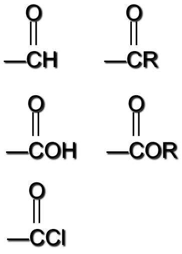
Electron-withdrawing Groups (EWGs) Destabilize Intermediates for ortho and para Substitution



$—CF_3$ is a powerful EWG. It is strongly deactivating and meta directing

Many EWGs Have a Carbonyl Group Attached Directly to the Ring

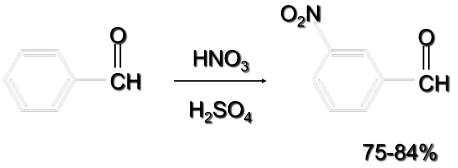
—EWG =

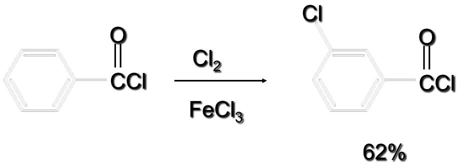


$—\overset{O}{\overset{\|}{C}}H \quad —\overset{O}{\overset{\|}{C}}R \quad —\overset{O}{\overset{\|}{C}}OH \quad —\overset{O}{\overset{\|}{C}}OR \quad —\overset{O}{\overset{\|}{C}}Cl$

All of these are meta directing and strongly deactivating

Nitration of Benzaldehyde





Other EWGs Include:

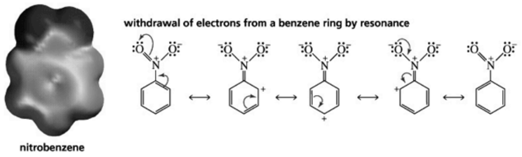
—EWG = $—NO_2$

$—SO_3H$

—C≡N

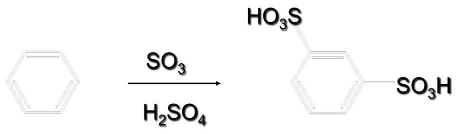
All of these are meta directing and strongly deactivating

Electron withdrawing by resonance:



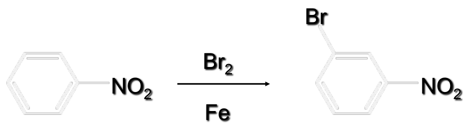
C=O, CN, and NO_2 also withdraw electrons by resonance

Disulfonation of Benzene



90%

Bromination of Nitrobenzene

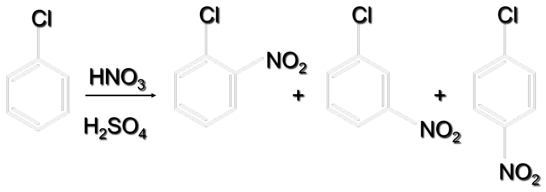


60-75%

Substituent Effects in Electrophilic
Aromatic Substitution:
Halogens

F, Cl, Br, and I are ortho-para directing, but deactivating

Nitration of Chlorobenzene



30% 1% 69%

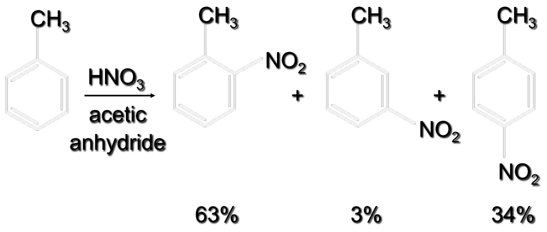
The rate of nitration of chlorobenzene is about 30 times slower than that of benzene.

Effect on Regioselectivity

Ortho-para directors direct an incoming electrophile to positions ortho and/or para to themselves.

Meta directors direct an incoming electrophile to positions meta to themselves.

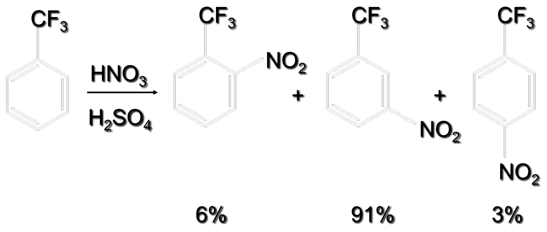
Nitration of Toluene



o- and *p*-nitrotoluene together comprise 97% of the product

a methyl group is an ortho-para director

Nitration of (Trifluoromethyl)benzene



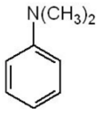
m-nitro(trifluoromethyl)benzene comprises 91% of the product

a trifluoromethyl group is a meta director

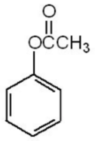
Question

- Arrange the compounds below in order of decreasing rate of chlorination.

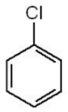
- A) 1 > 2 > 3
- B) 2 > 3 > 1
- C) 3 > 2 > 1
- D) 1 > 3 > 2



1



2

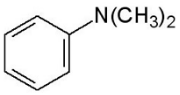


3

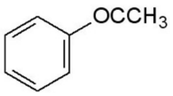
Question

- Which compound will add a nitro group to the meta position?

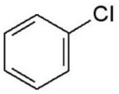
- A)



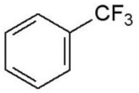
B)



- C)

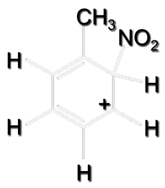


D)

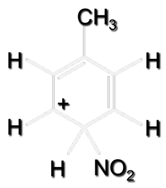


Rate and Regioselectivity
in the
Nitration of Toluene

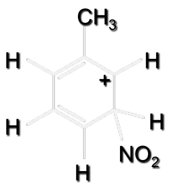
Carbocation Stability Controls Regioselectivity



gives ortho

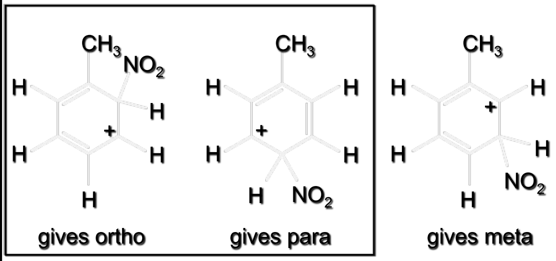


gives para



gives meta

Carbocation Stability Controls Regioselectivity



gives ortho gives para gives meta

more stable less stable

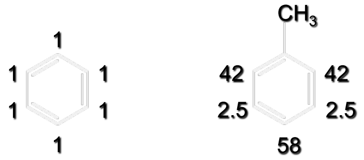
Nitration of Toluene: Interpretation

- The rate-determining intermediates for ortho and para nitration each have a resonance form that is a tertiary carbocation. All of the resonance forms for the rate -determining intermediate in meta nitration are secondary carbocations.
- Tertiary carbocations, being more stable, are formed faster than secondary ones. Therefore, the intermediates for attack at the ortho and para positions are formed faster than the intermediate for attack at the meta position. This explains why the major products are *o*- and *p*-nitrotoluene.

Nitration of Toluene: Partial Rate Factors

- The experimentally determined reaction rate can be combined with the ortho/meta/para distribution to give *partial rate factors* for substitution at the various ring positions.
- Expressed as a numerical value, a partial rate factor tells you by how much the rate of substitution at a particular position is faster (or slower) than at a single position of benzene.

Nitration of Toluene: Partial Rate Factors



All of the available ring positions in toluene are more reactive than a single position of benzene.

A methyl group activates all of the ring positions but the effect is greatest at the ortho and para positons.

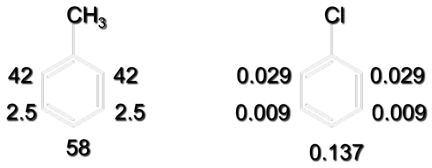
Steric hindrance by the methyl group makes each ortho position slightly less reactive than para.

Nitration of Toluene vs. tert-Butylbenzene

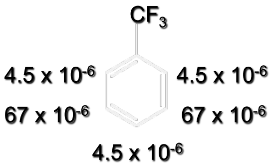
tert-Butyl is activating and ortho-para directing

tert-Butyl crowds the ortho positions and decreases the rate of attack at those positions.

Nitration of Toluene vs. Chlorobenzene



Nitration of (Trifluoromethyl)benzene: Partial Rate Factors

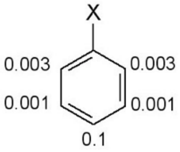


All of the available ring positions in (trifluoromethyl)benzene are much less reactive than a single position of benzene.

A CF_3 group deactivates all of the ring positions but the degree of deactivation is greatest at the ortho and para positons.

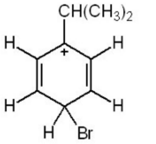
Question

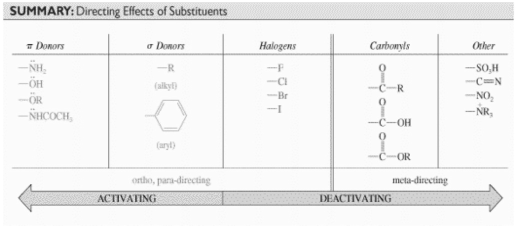
- Which is the most likely candidate for substituent X based on the partial rate factors for nitration given beside the structural formula?
- A) $-OCH_3$
- B) -CH=O
- C) $-SO_3H$
- D) -Br



Question

- Which reactants combine to
- give the species shown a
- the right as a reactive
- intermediate?
-
- A) Benzene, isopropyl bromide, and HBr
- B) Bromobenzene, isopropyl chloride, and $AlCl_3$
- C) Isopropylbenzene, Br_2, $FeBr_3$
- D) Isopropylbenzene, light, and heat



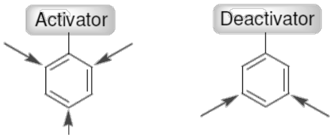


SUMMARY: Directing Effects of Substituents

π Donors	*σ Donors*	*Halogens*	*Carbonyls*	*Other*
$-\ddot{N}H_2$ $-\ddot{O}H$ $-\ddot{O}R$ $-\ddot{N}HCOCH_3$	—R (alkyl) (aryl)	—F —Cl —Br —I	$-C(=O)-R$ $-C(=O)-OH$ $-C(=O)-OR$	$-SO_3H$ $-C\equiv N$ $-NO_2$ $-\overset{+}{N}R_3$

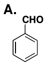
ortho, para-directing | meta-directing

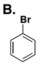
ACTIVATING | DEACTIVATING

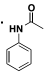


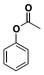
Question

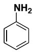
Identify the following as activating (I) or deactivating (II) and as ortho-para (III) or meta directors (IV).

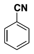
A.


B.


C.


D.


E.


F.


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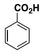

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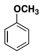


A. I = A, B, F, G; II = C, D, E, H; III = B, C, D, E, H; IV = A, F, G

B. I = A, B, F, G; II = C, D, E, H; III = A, F, G; IV = B, C, D, E, H

C. I = C, D, E, H; II = A, B, F, G; III = A, F, G; IV = B, C, D, E, H

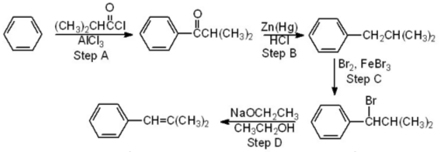
D. I = C, D, E, H; II = A, B, F, G; III = B, C, D, E, H; IV = A, F, G

Question

- Which of the following statements is false?
- A) All activating groups are ortho, para directors.
- B) Halogen substituents are slightly deactivating, but are ortho, para directing.
- C) Strongly activating substances are meta directors.
- D) Some of the most powerful activating substances are those with an oxygen directly attached to the ring.

Question

- Which step is incorrect in respect to its major organic product? Give the letter
- corresponding to the first incorrect step.



- A) Step A B) Step B
- C) Step C D) Step D