Electrophilic Aromatic Substitution

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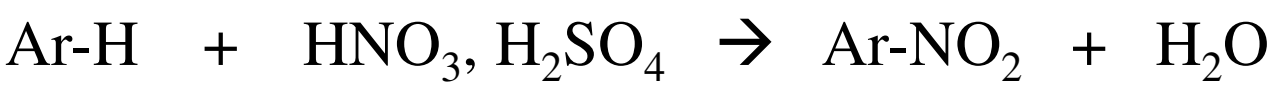
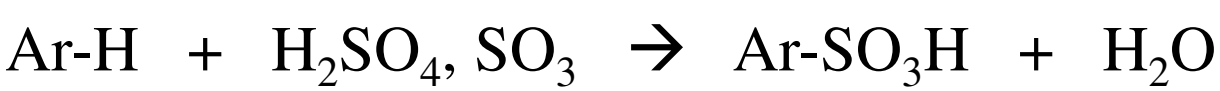
Electrophilic Aromatic Substitution (Aromatic compounds)

Ar-H = aromatic compound

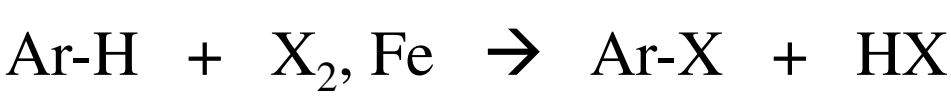
1. Nitration



2. Sulfonation



3. Halogenation



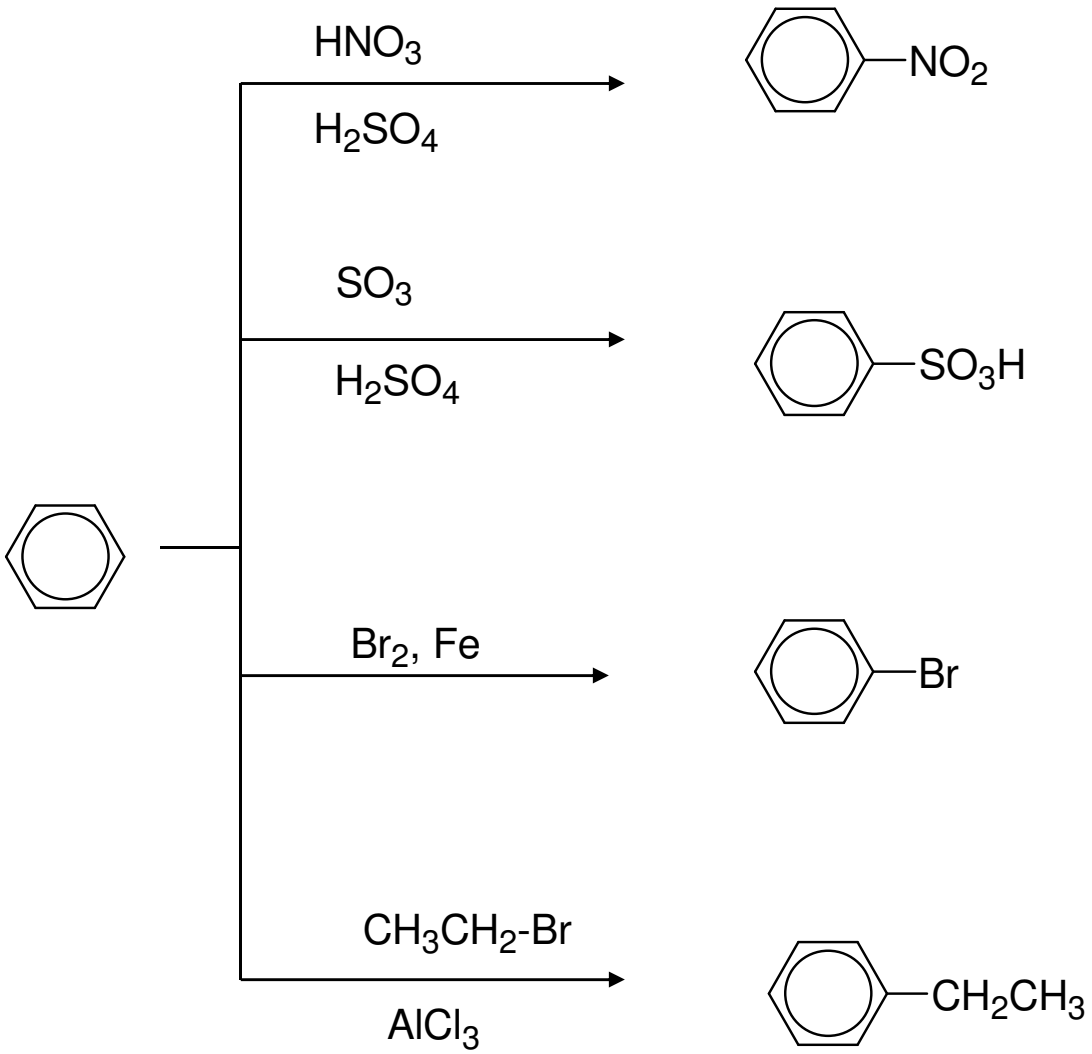
4. Friedel-Crafts alkylation

Friedel-Crafts alkylation (variations)

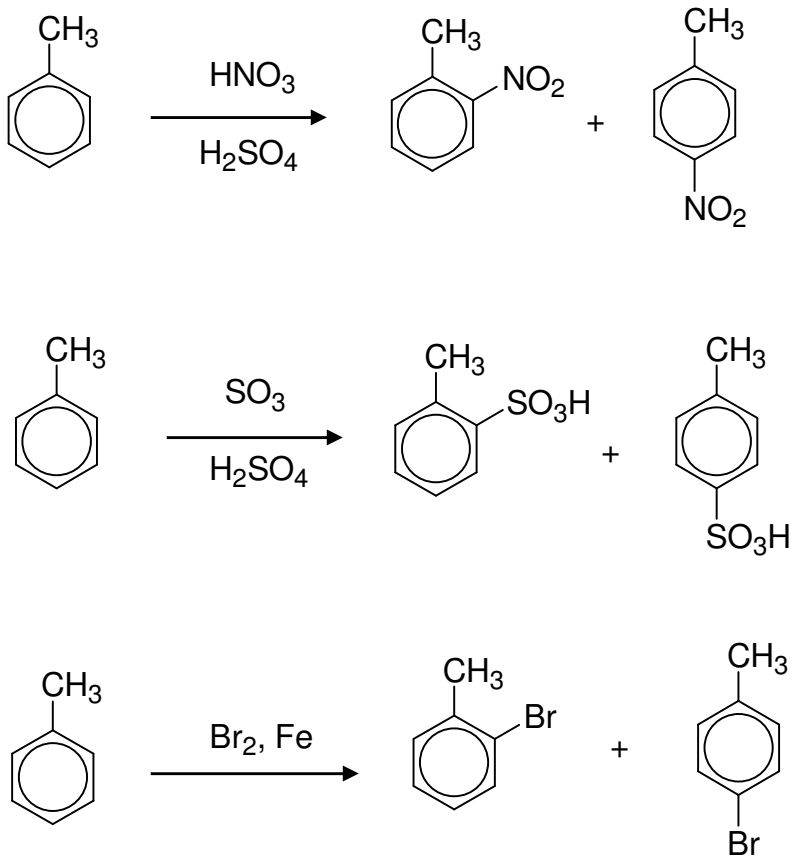
a) $Ar\text{-}H + R\text{-}X, AlCl_3 \rightarrow Ar\text{-}R + HX$

b) $Ar\text{-}H + R\text{-}OH, H^+ \rightarrow Ar\text{-}R + H_2O$

c) $Ar\text{-}H + Alkene, H^+ \rightarrow Ar\text{-}R$

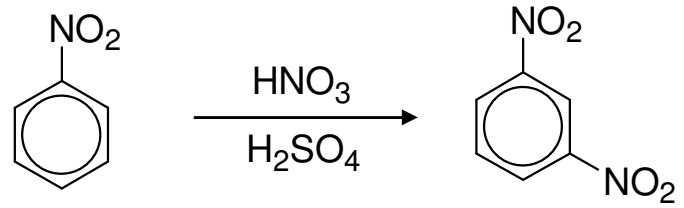

HNO3
H2SO4
NO2
SO3
H2SO4
SO3H
Br2, Fe
Br
CH3CH2-Br
AlCl3
CH2CH3

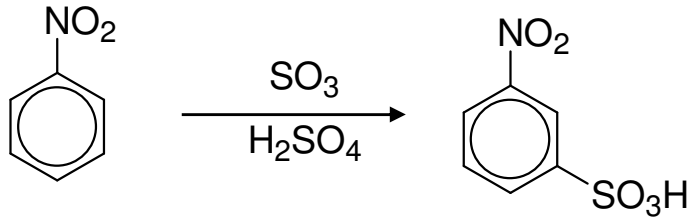
toluene

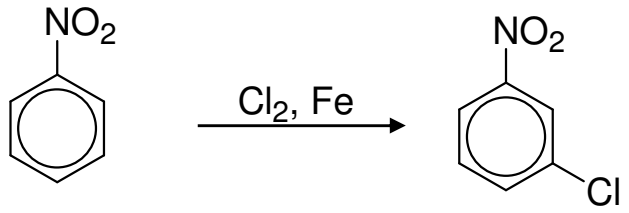


faster than the same reactions with benzene

nitrobenzene







slower than the same reactions with benzene

Substituent groups on a benzene ring affect electrophilic aromatic substitution reactions in two ways:

1) **reactivity**

activate (faster than benzene)

or deactivate (slower than benzene)

2) **orientation**

ortho- + *para*- direction

or *meta*- direction

-CH_3

activates the benzene ring towards EAS

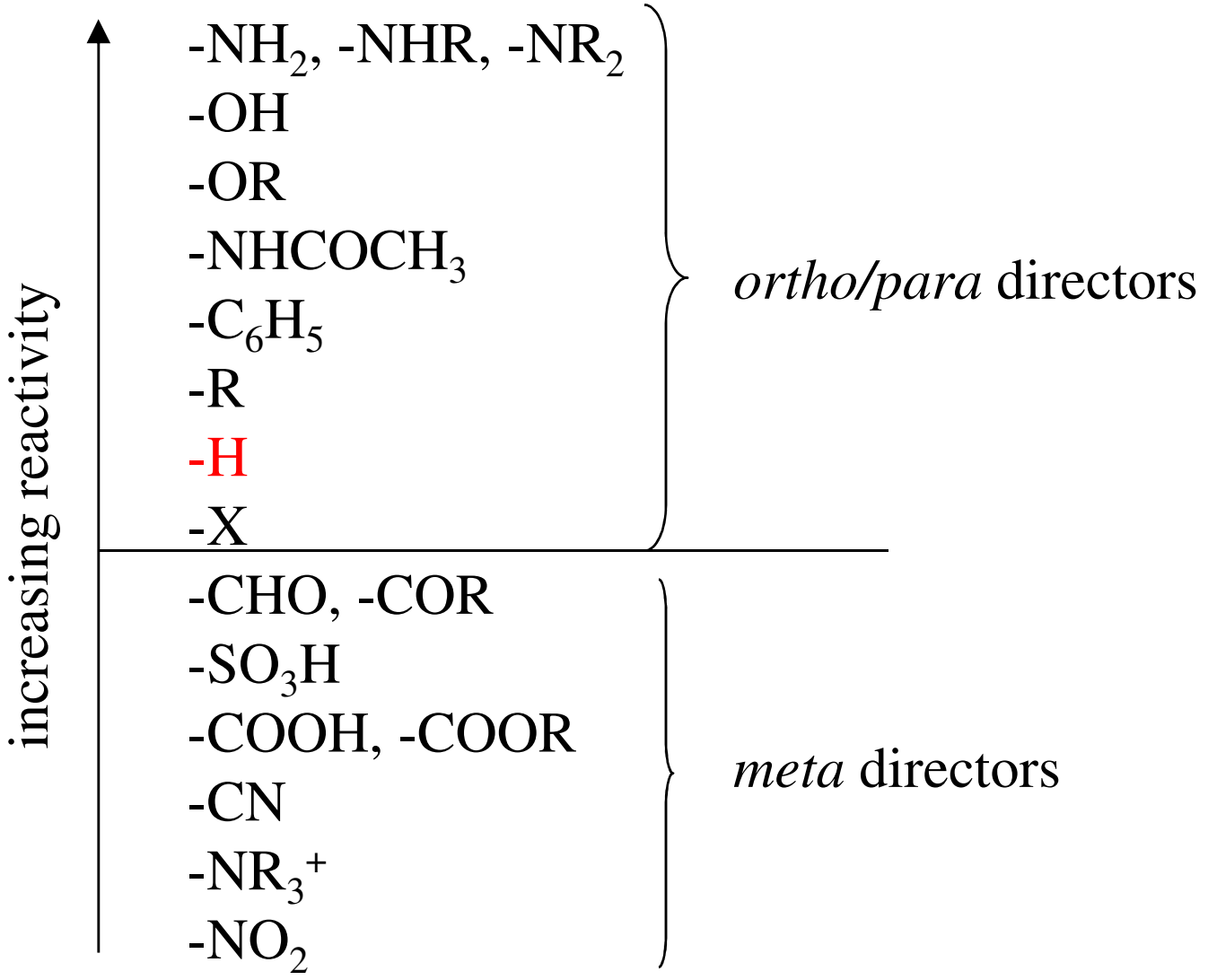
directs substitution to the *ortho-* & *para-* positions

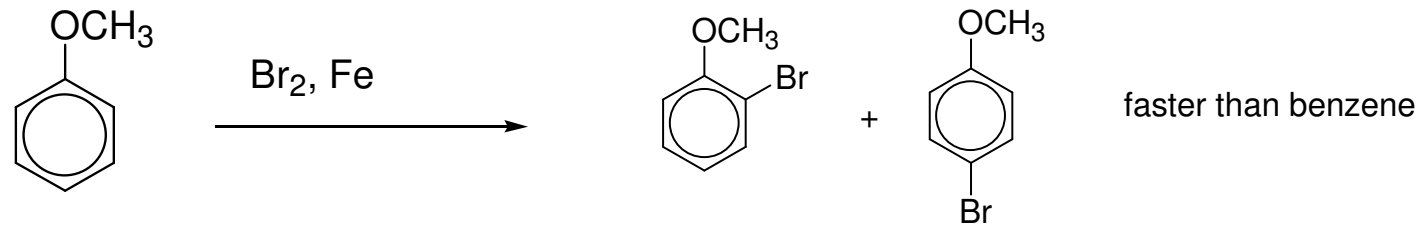
-NO_2

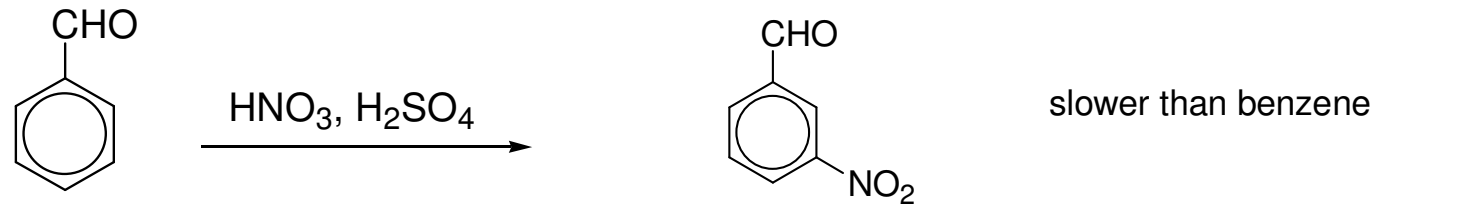
deactivates the benzene ring towards EAS

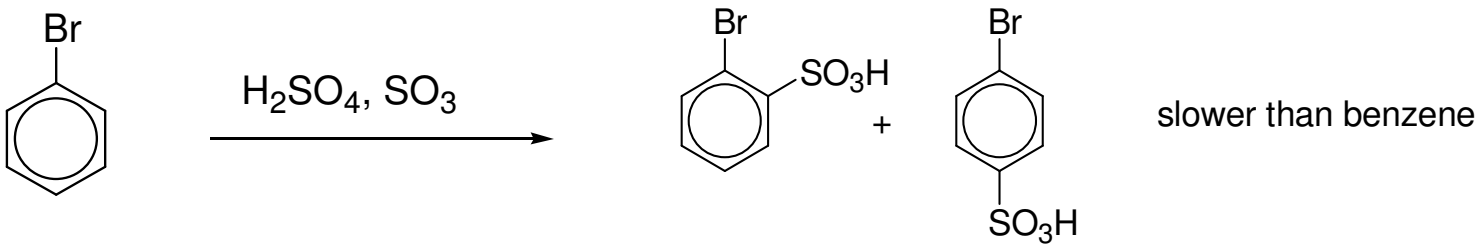
directs substitution to the *meta-* position

Common substituent groups and their effect on EAS:



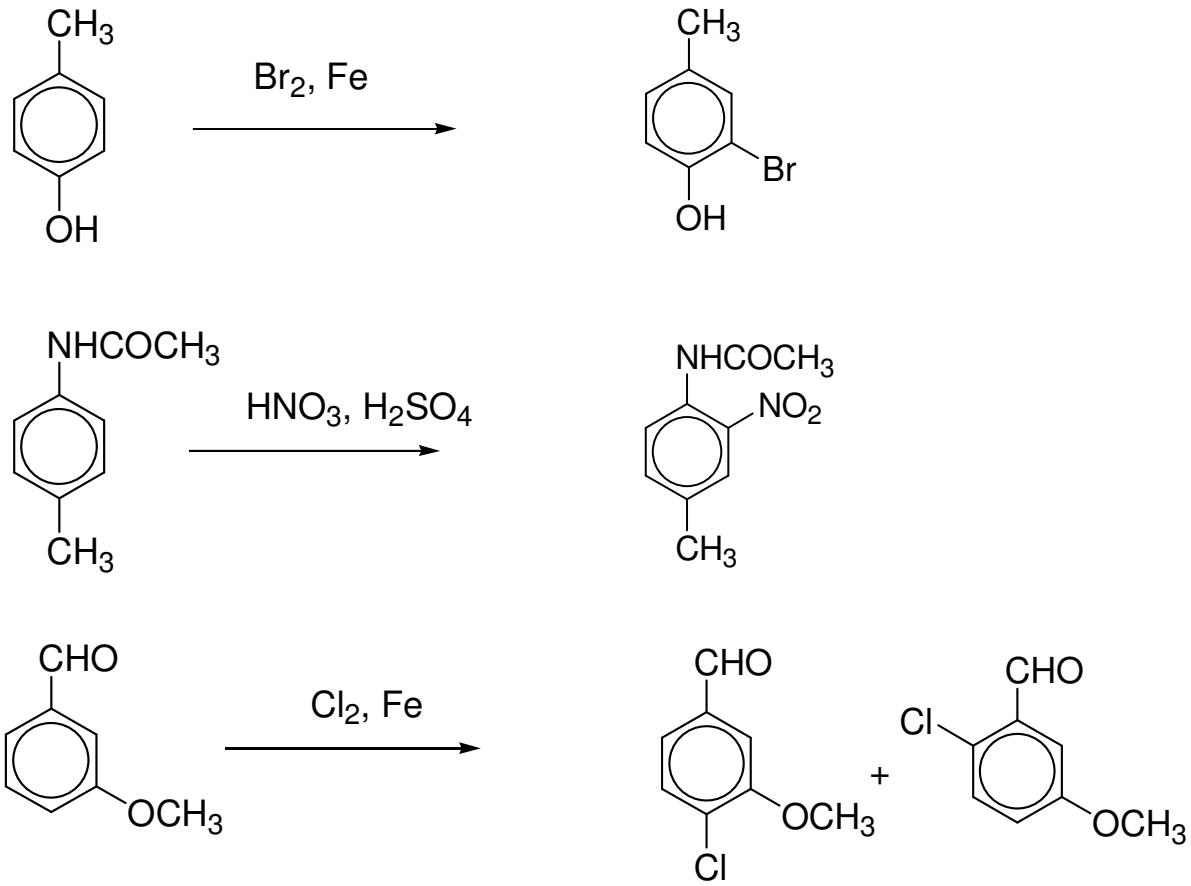

OCH3
Br2, Fe
OCH3
Br
+
OCH3
Br
faster than benzene


CHO
HNO3, H2SO4
CHO
NO2
slower than benzene


Br
H2SO4, SO3
Br
SO3H
+
Br
SO3H
slower than benzene

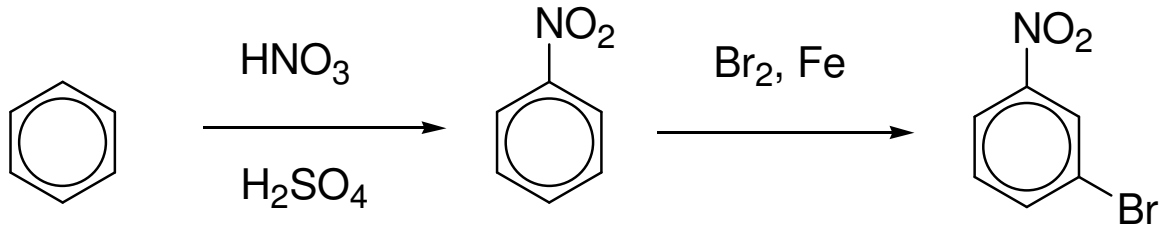
If there is more than one group on the benzene ring:

1. The group that is more activating (higher on “the list”) will direct the next substitution.
2. You will get little or no substitution between groups that are *meta*- to each other.

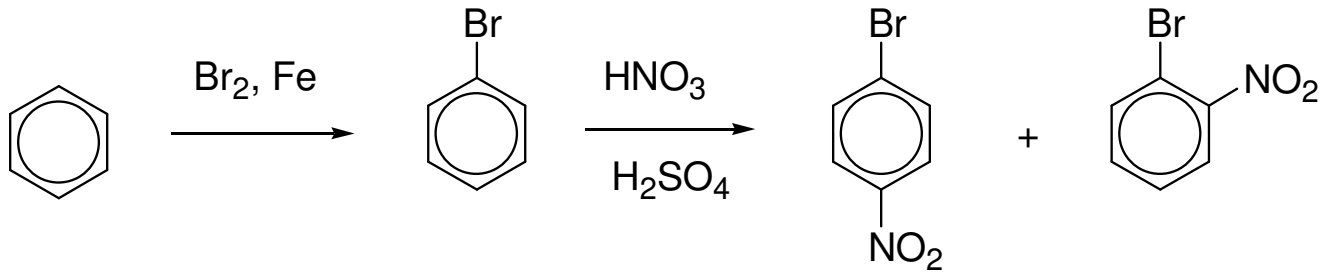

CH3
OH
Br2, Fe
CH3
Br
OH
NHCOCH3
CH3
HNO3, H2SO4
NHCOCH3
NO2
CH3
CHO
OCH3
Cl2, Fe
CHO
OCH3
Cl
+
CHO
Cl
OCH3

Orientation and synthesis. Order is important!

synthesis of *m*-bromonitrobenzene from benzene:



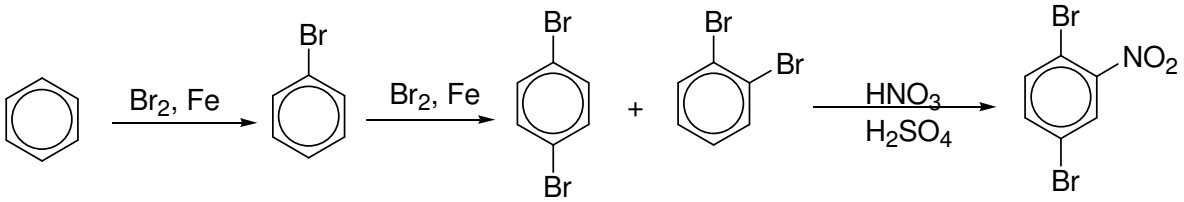
synthesis of *p*-bromonitrobenzene from benzene:



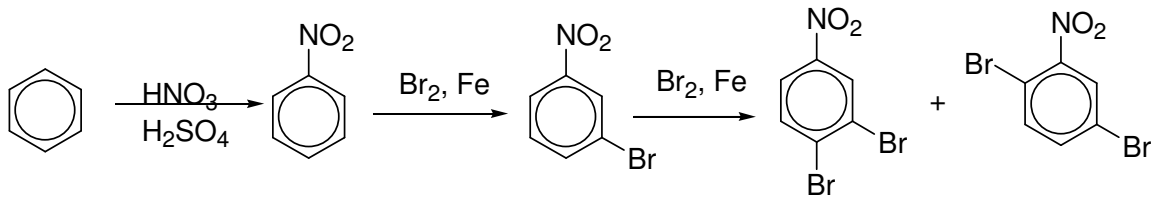
You may assume that you can separate a pure *para*-isomer from an *ortho*-/*para*- mixture.

note: the assumption that you can separate a pure para isomer from an ortho/para mixture does not apply to any other mixtures.

synthesis of 1,4-dibromo-2-nitrobenzene from benzene

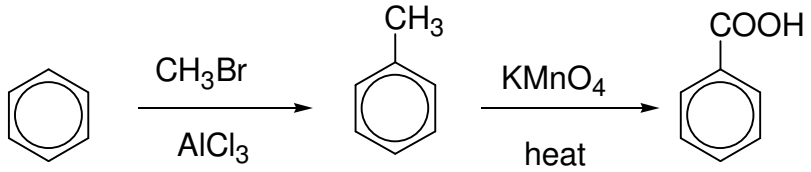


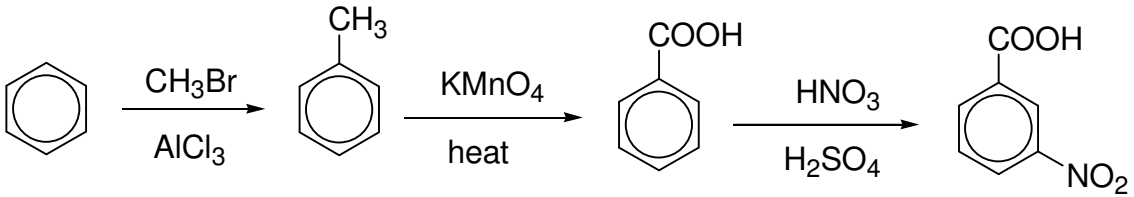
separate pure para isomer from ortho/para mixture

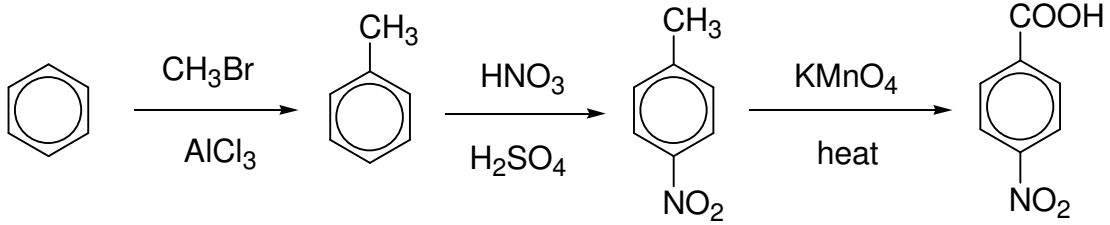


cannot assume that these can be separated!

synthesis of benzoic acids by oxidation of $-CH_3$







+ ortho-

Links to problem sets on the web involving EAS:

http://chemistry2.csudh.edu/organic/aromatics/reactions.html

Reactivity and sites on monosubstituted benzene
Reaction Sties on disubstituted benzenes
Synthesis of disubstituted benzenes
Synthesis of trisubstituited benzenes

nitration

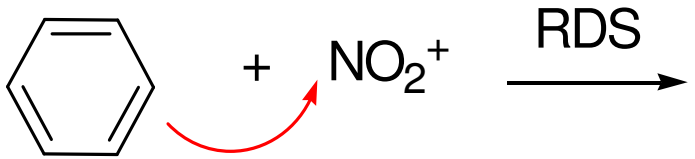
$$\begin{aligned}
&HO\text{-}NO_2 + H_2SO_4 \leftrightarrows H_2\overset{+}{O}\text{-}NO_2 + HSO_4^- \\
&H_2\overset{+}{O}\text{-}NO_2 \leftrightarrows H_2O + \overset{+}{N}O_2 \\
&H_2SO_4 + H_2O \leftrightarrows HSO_4^- + H_3O^+
\end{aligned}$$

$$HNO_3 + 2\,H_2SO_4 \leftrightarrows H_3O^+ + 2\,HSO_4^- + NO_2^+$$

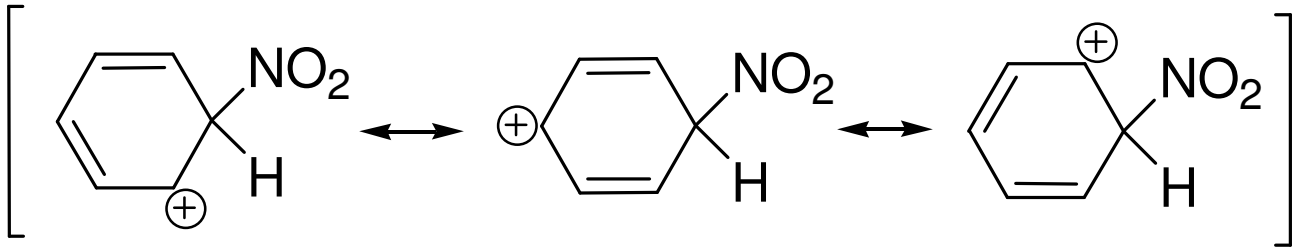
nitration:

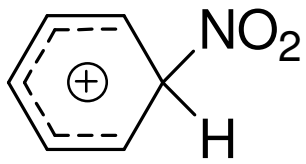
1) $HONO_2 + 2\,H_2SO_4 \rightleftharpoons H_3O^+ + 2\,HSO_4^- + NO_2^+$

electrophile

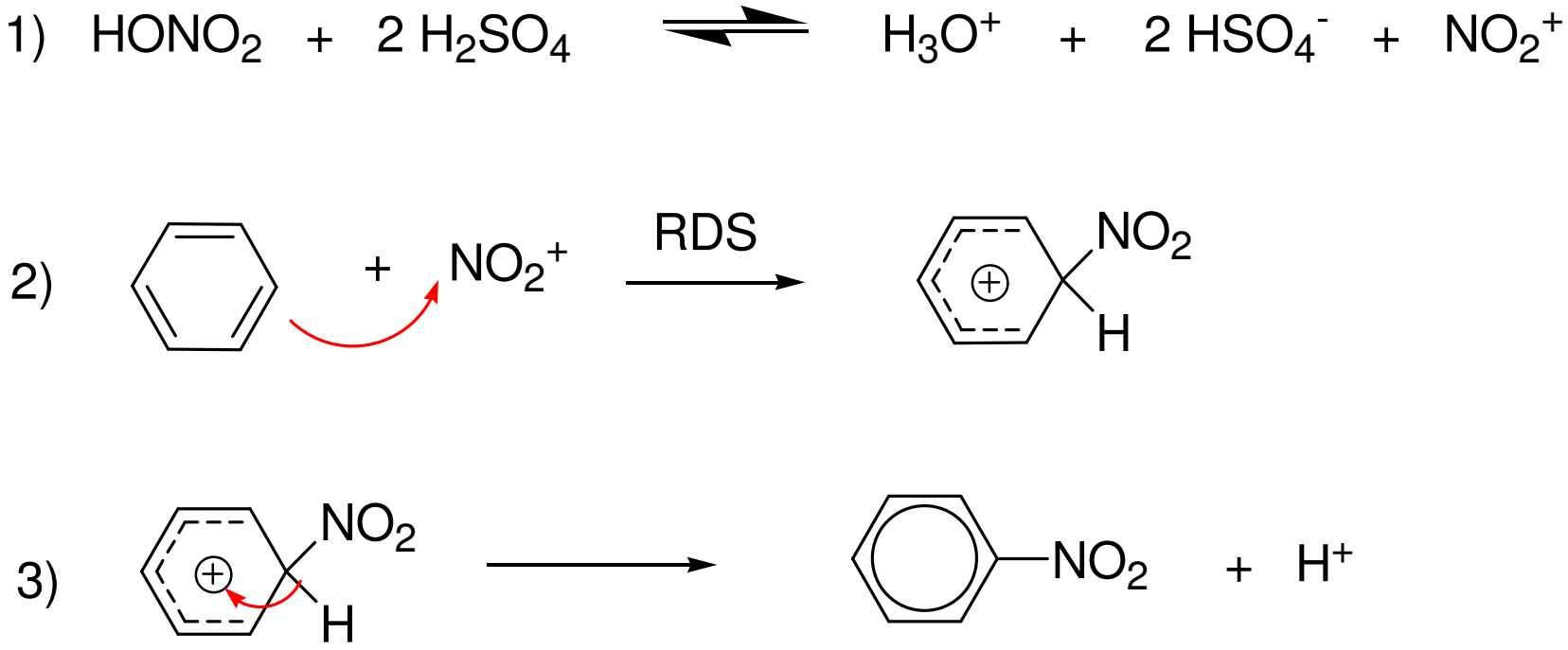
2) 

resonance

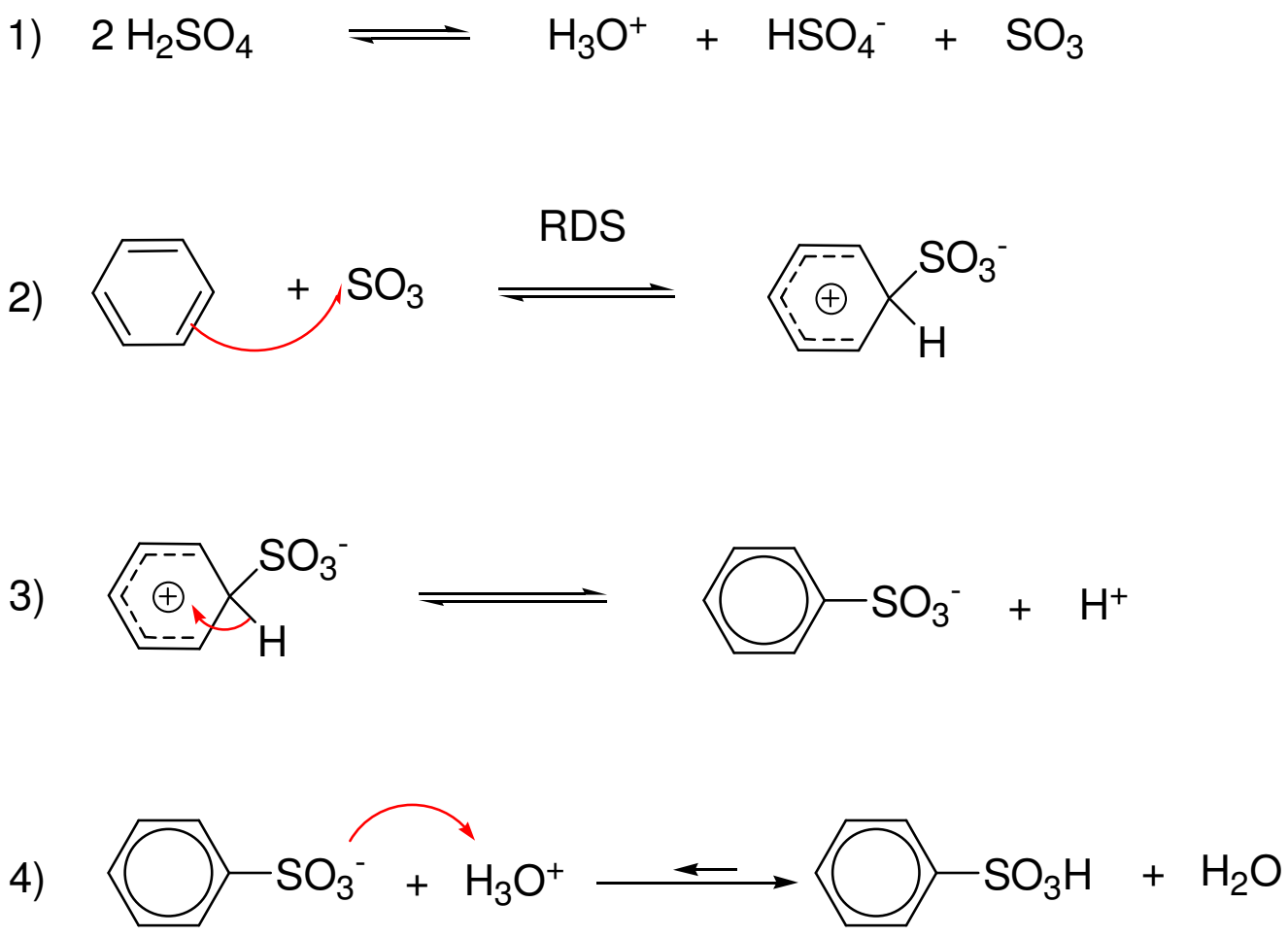




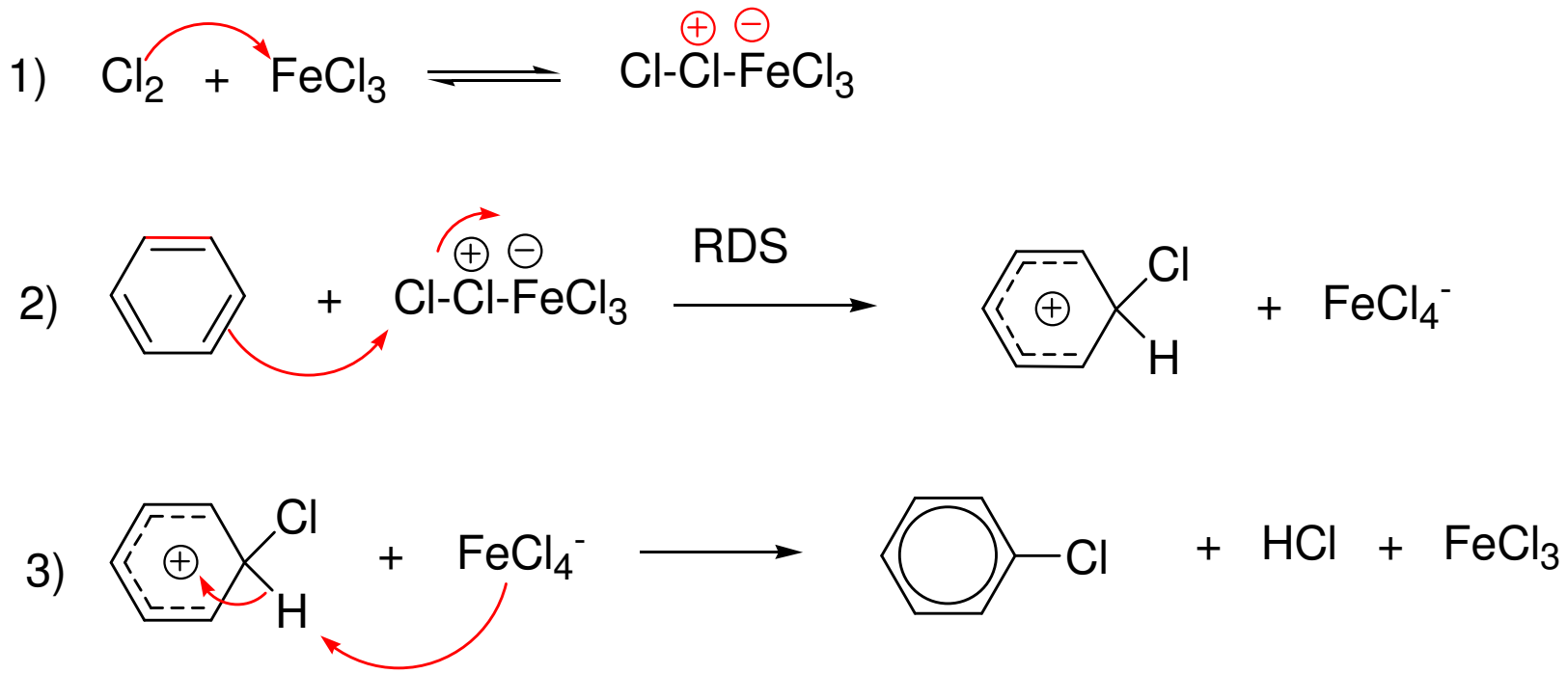
Mechanism for nitration:



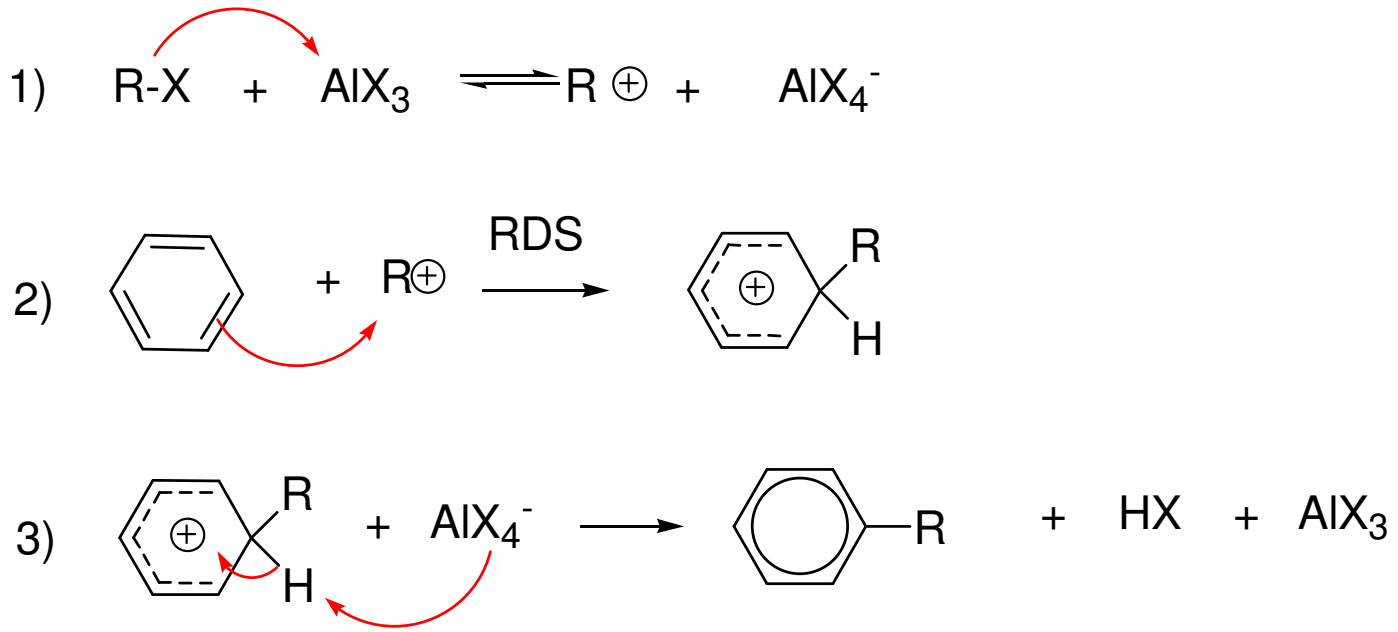
Mechanism for sulfonation:



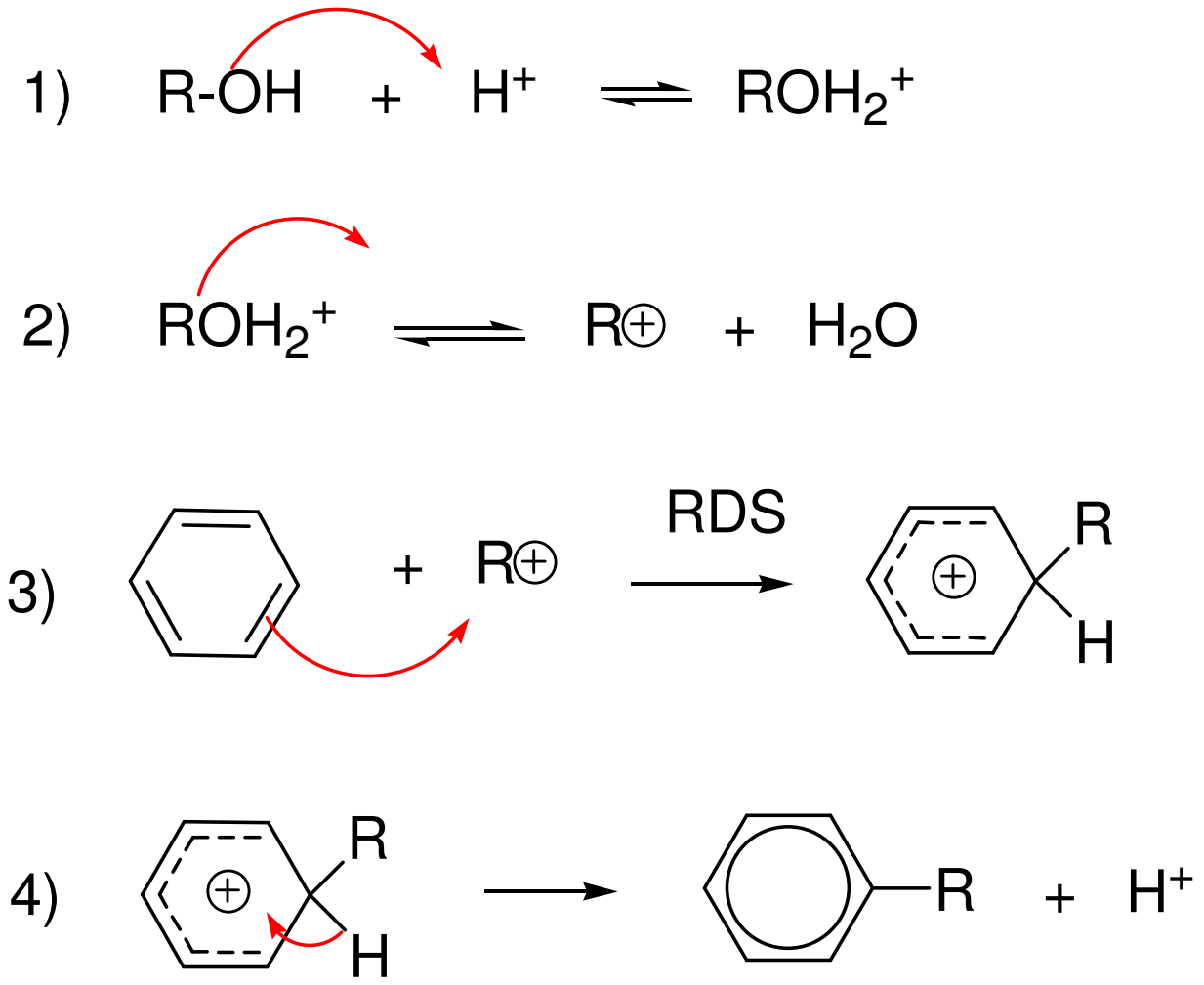
Mechanism for halogenation:



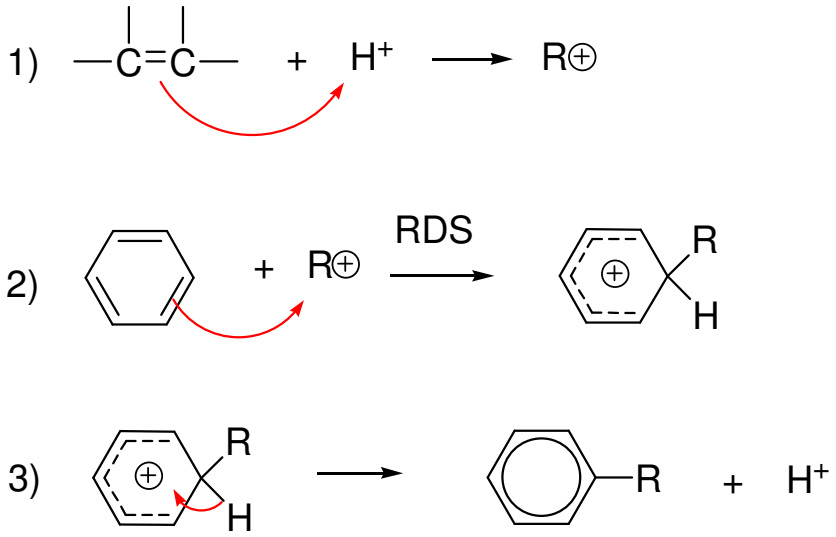
Mechanism for Friedel-Crafts alkylation:



Mechanism for Friedel-Crafts with an alcohol & acid

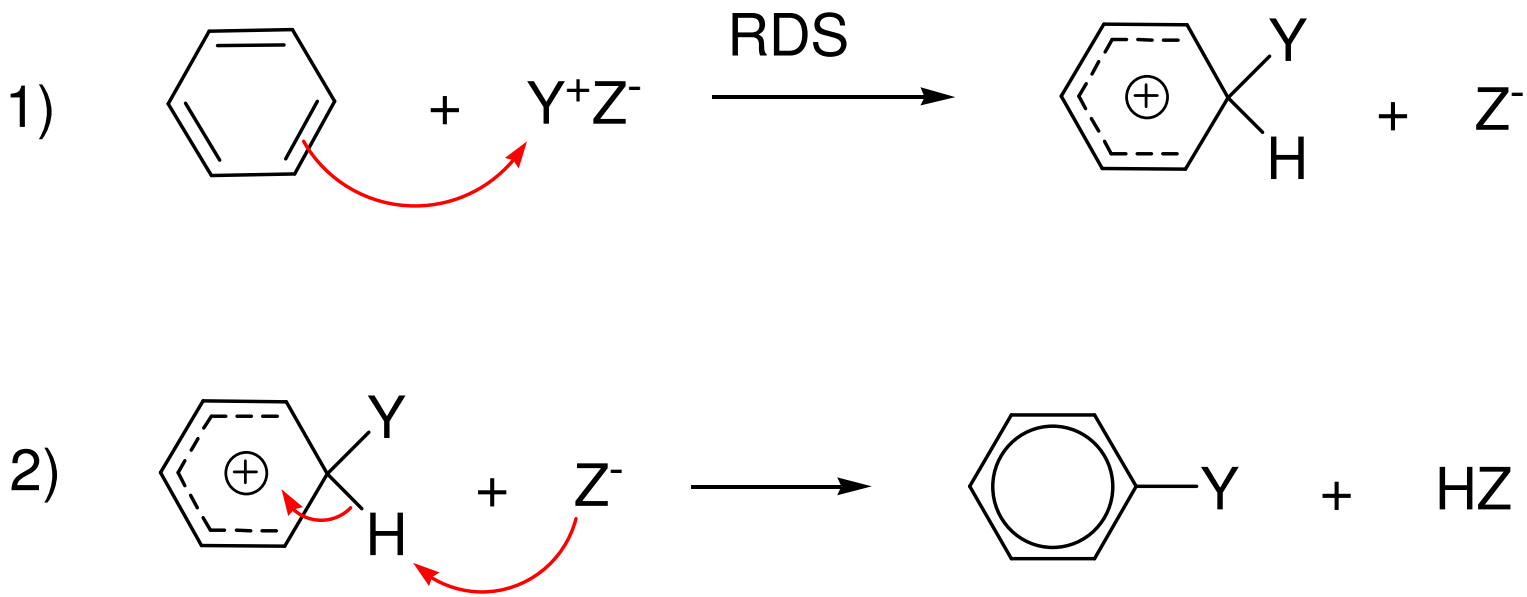


Mechanism for Friedel-Crafts with alkene & acid:



electrophile in Friedel-Crafts alkylation = carbocation

“Generic” Electrophilic Aromatic Substitution mechanism:



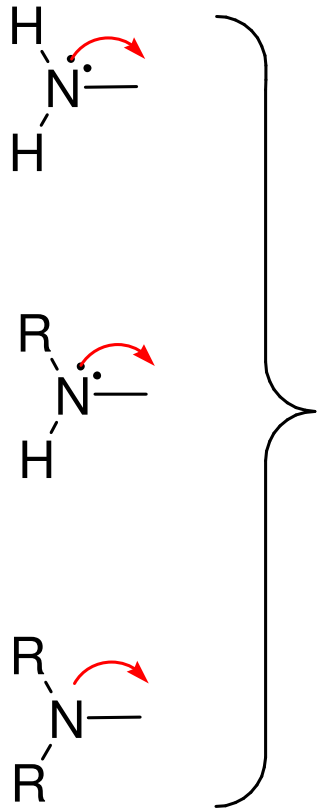
Why do substituent groups on a benzene ring affect the reactivity and orientation in the way they do?

→ electronic effects, "pushing" or "pulling" electrons by the substituent.

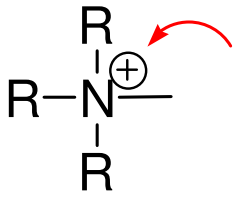
Electrons can be donated ("pushed") or withdrawn ("pulled") by atoms or groups of atoms via:

Induction – due to differences in electronegativities

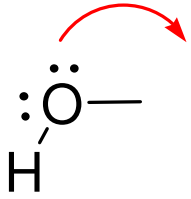
Resonance – delocalization via resonance



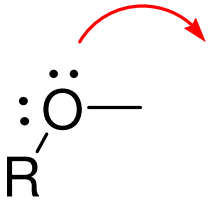
unshared pair of electrons on the nitrogen
resonance donating groups
(weaker inductive withdrawal)



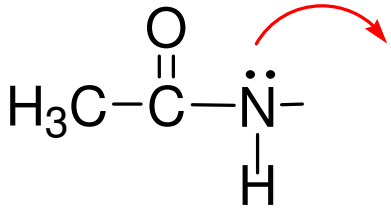
strong **inductive withdrawal**
(no unshared pair of electrons on the nitrogen & no resonance possible



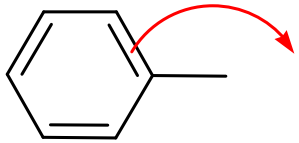
resonance donation
(weaker inductive withdrawal)



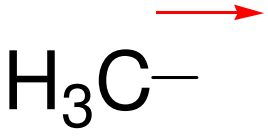
resonance donation
(weaker inductive withdrawal)



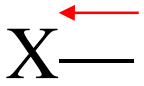
resonance donation
(weaker inductive withdrawal)



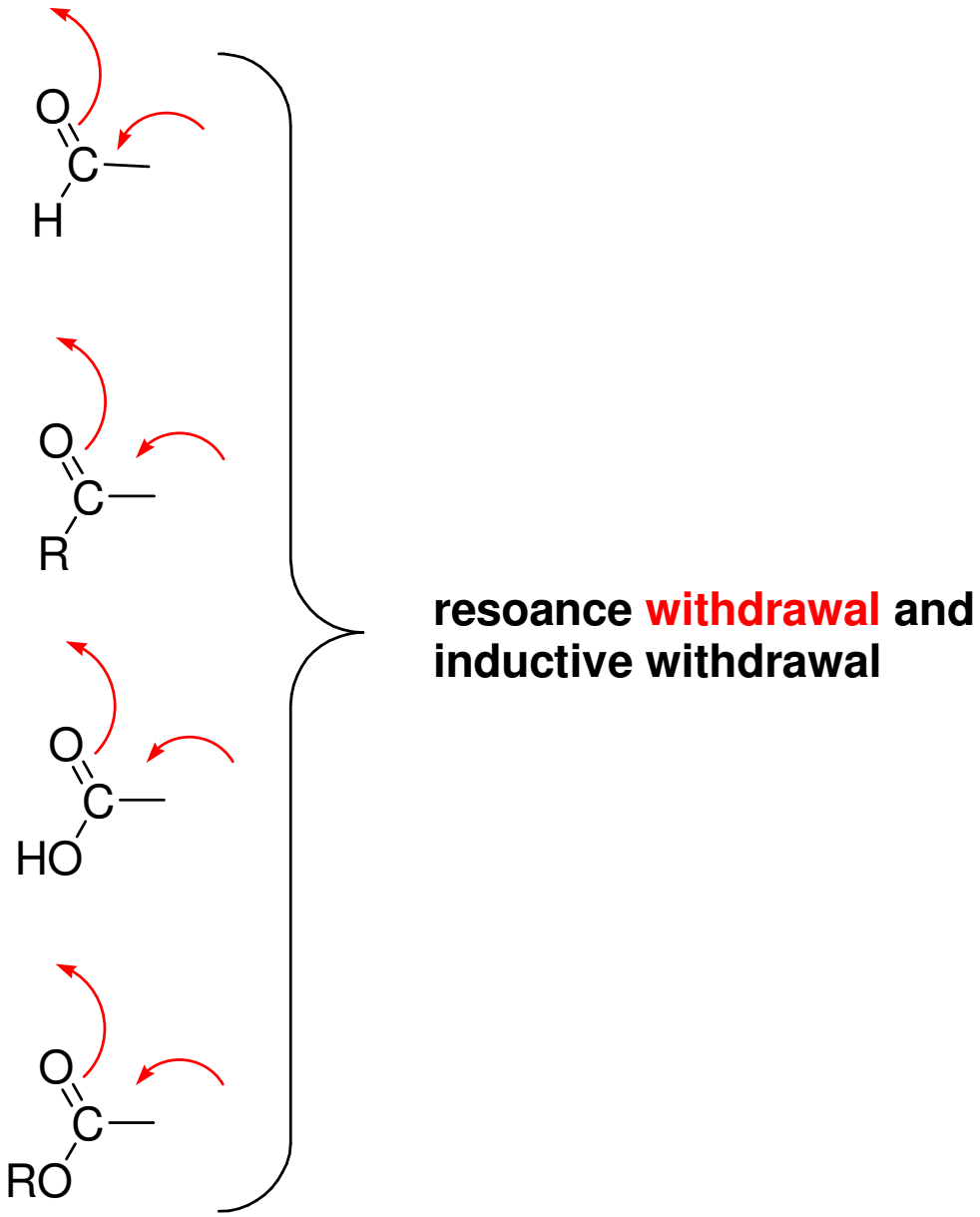
resonance donation



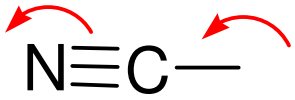
inductive donation
sp3 sp2 ring carbon



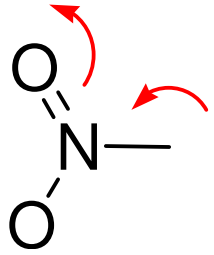
inductive withdrawal



resoance withdrawal and inductive withdrawal

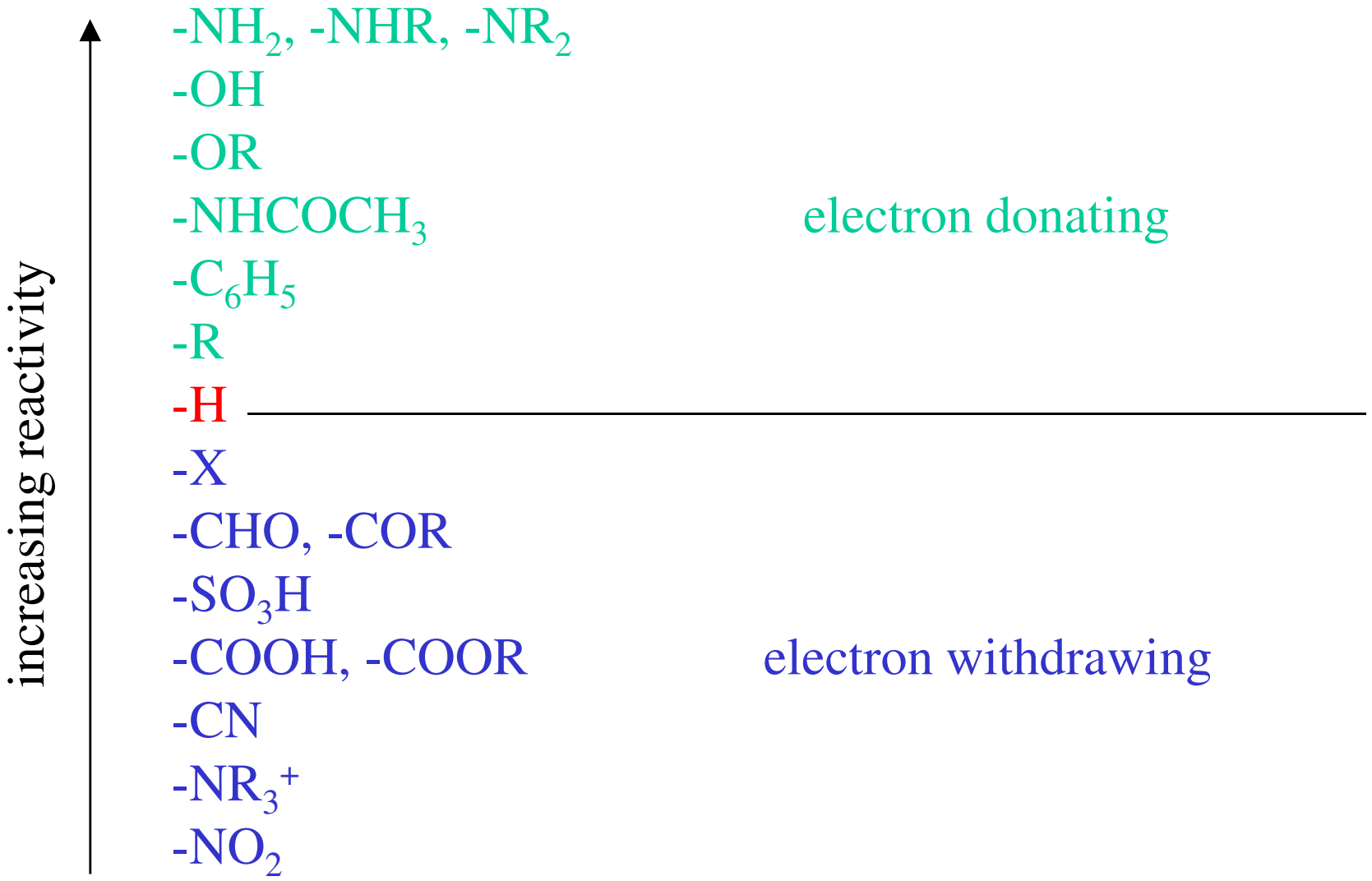


resonance and inductive withdrawal



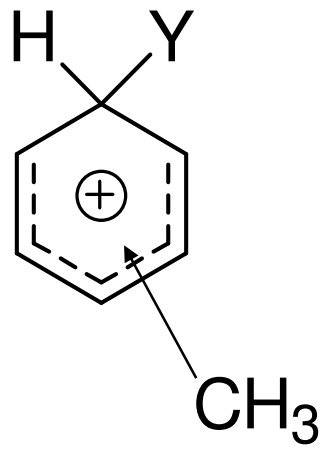
resonance and inductive withdrawal

Common substituent groups and their effect on reactivity in EAS:



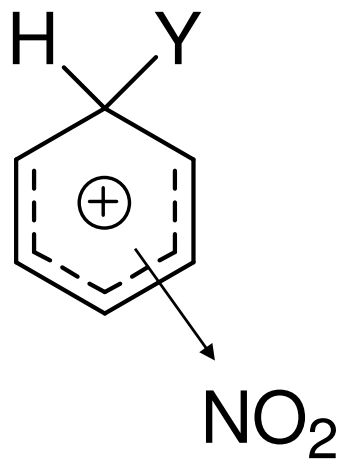
Electron donating groups activate the benzene ring to electrophilic aromatic substitution.

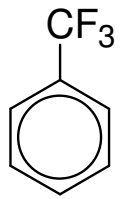
1. electron donating groups increase the electron density in the ring and make it more reactive with electrophiles.
2. electron donation stabilizes the intermediate carbocation, lowers the Eact and increases the rate.



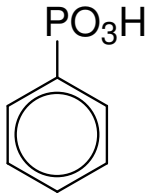
Electron withdrawing groups deactivate the benzene ring to electrophilic aromatic substitution.

1. electron withdrawing groups decrease the electron density in the ring and make it less reactive with electrophiles.
2. electron withdrawal destabilizes the intermediate carbocation, raising the Eact and slowing the rate.

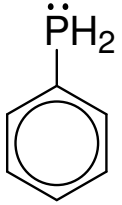




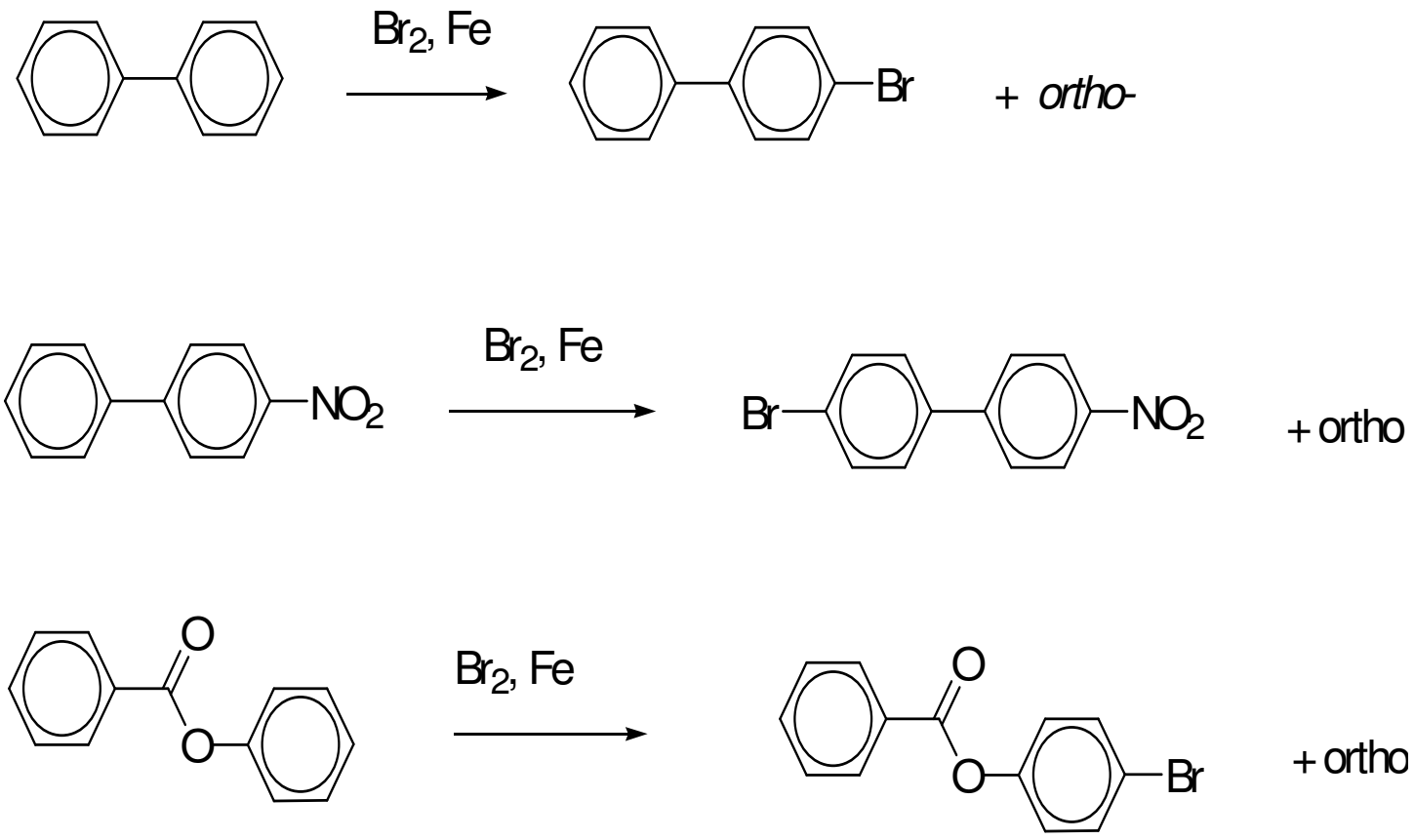
electron withdrawing = deactivating & *meta*-director



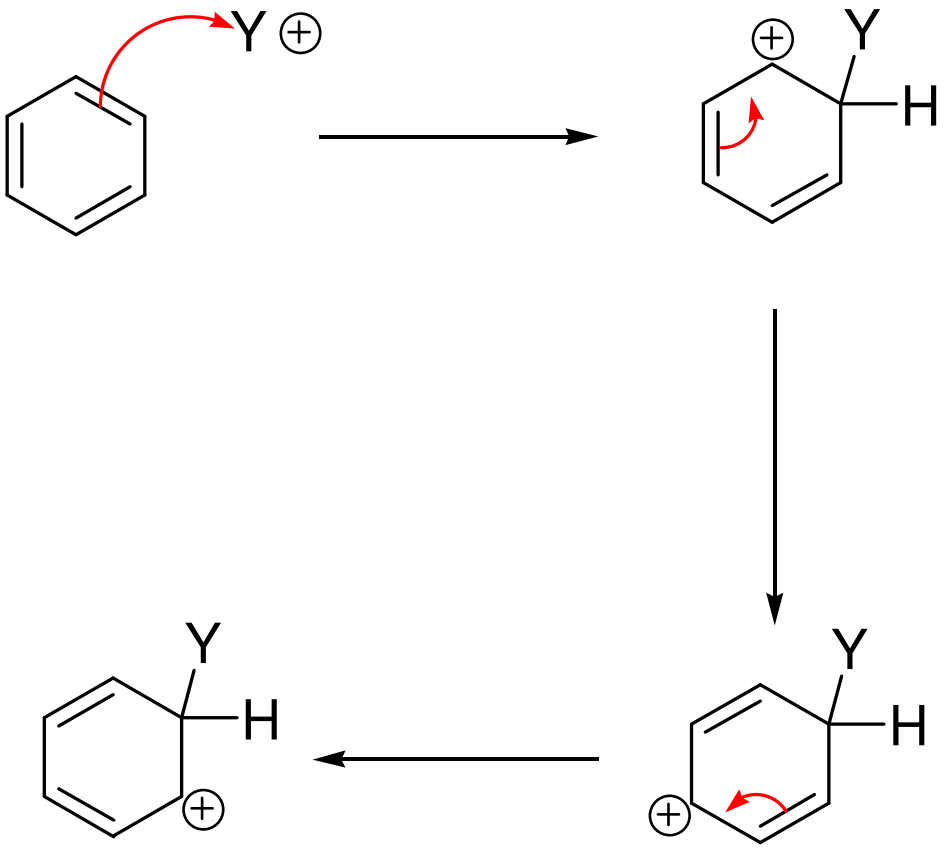
electron withdrawing = deactivating & *meta*-director

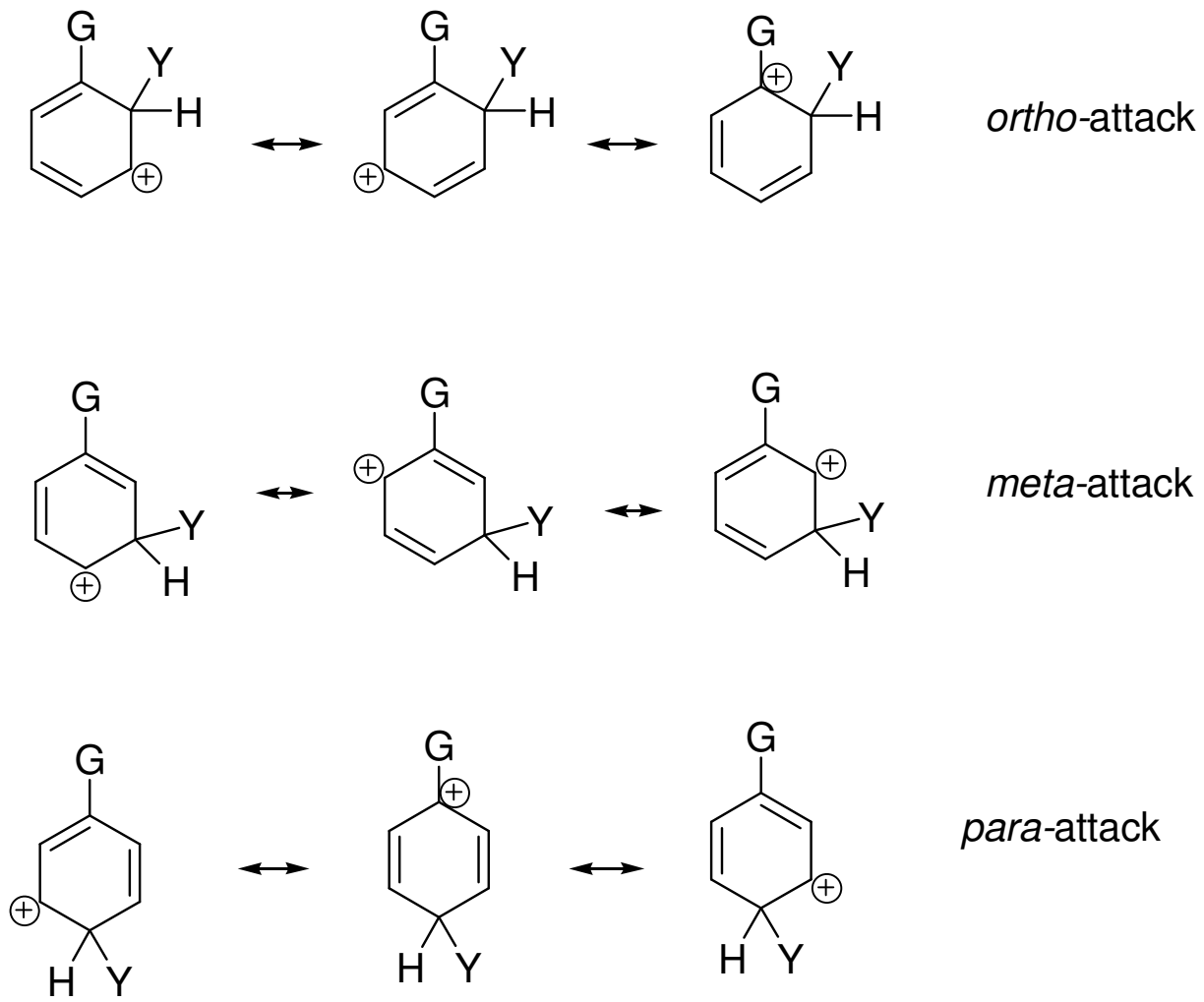


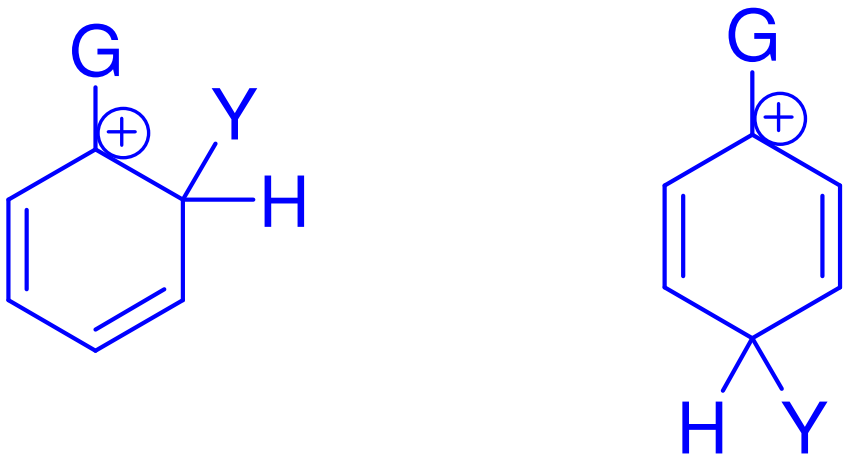
electron donating = activating & *ortho-/para*-director


Br2, Fe
Br
+ ortho-
Br2, Fe
NO2
Br
NO2
+ ortho
O
O
Br2, Fe
O
O
Br
+ ortho

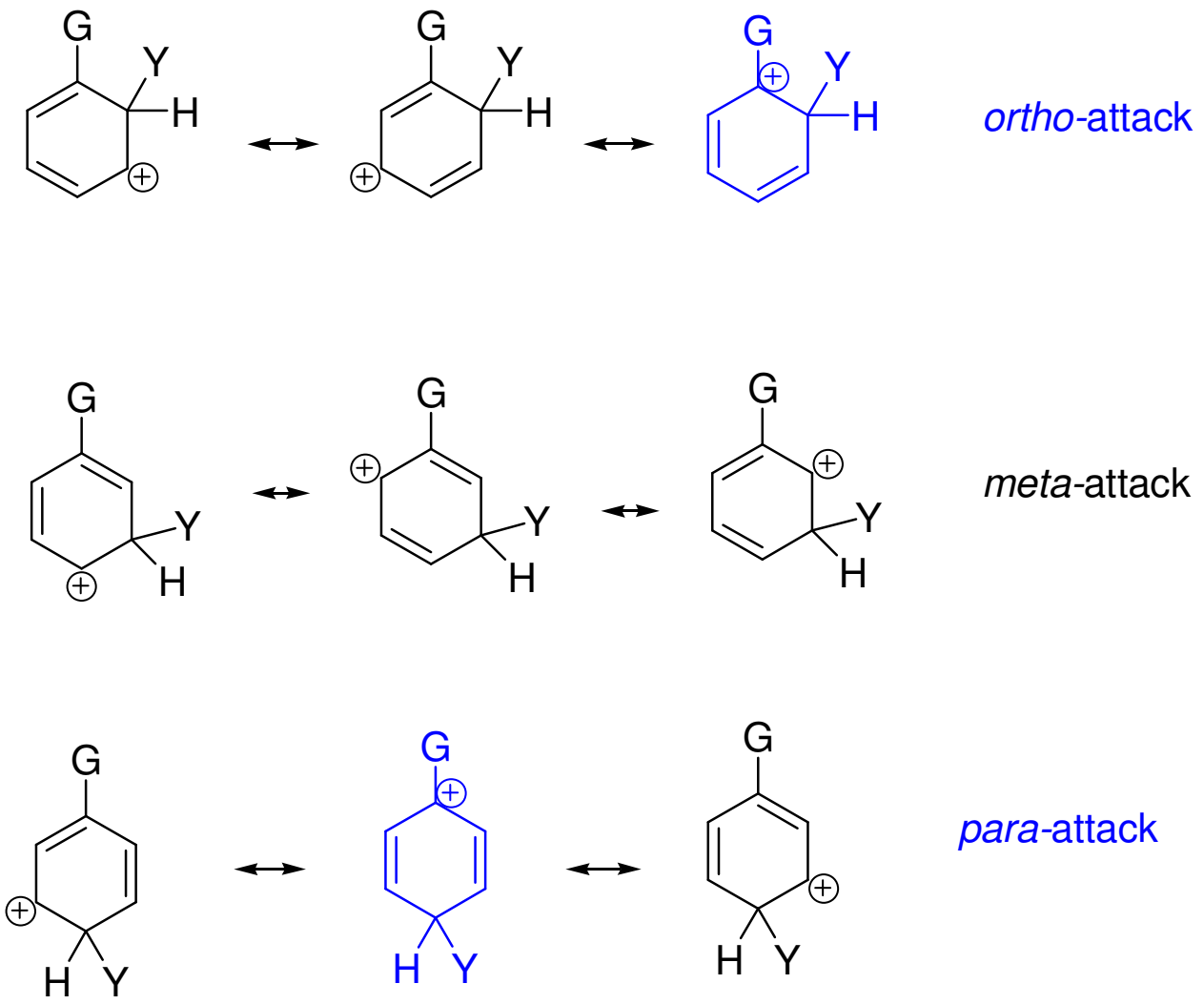
How to draw resonance structures for EAS




G
Y
H
ortho-attack
meta-attack
para-attack

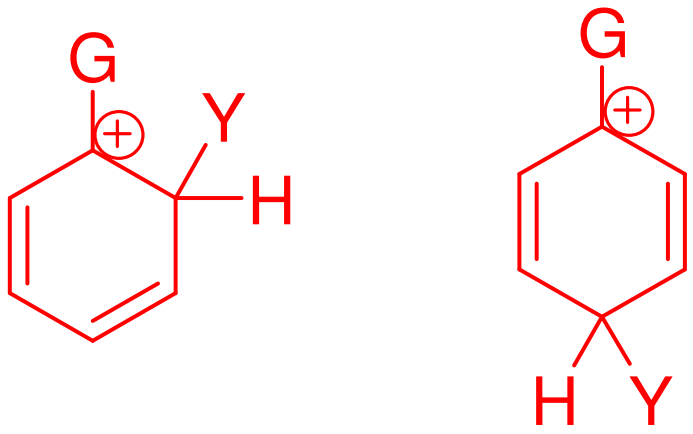


If G is an electron donating group, these structures are especially stable.

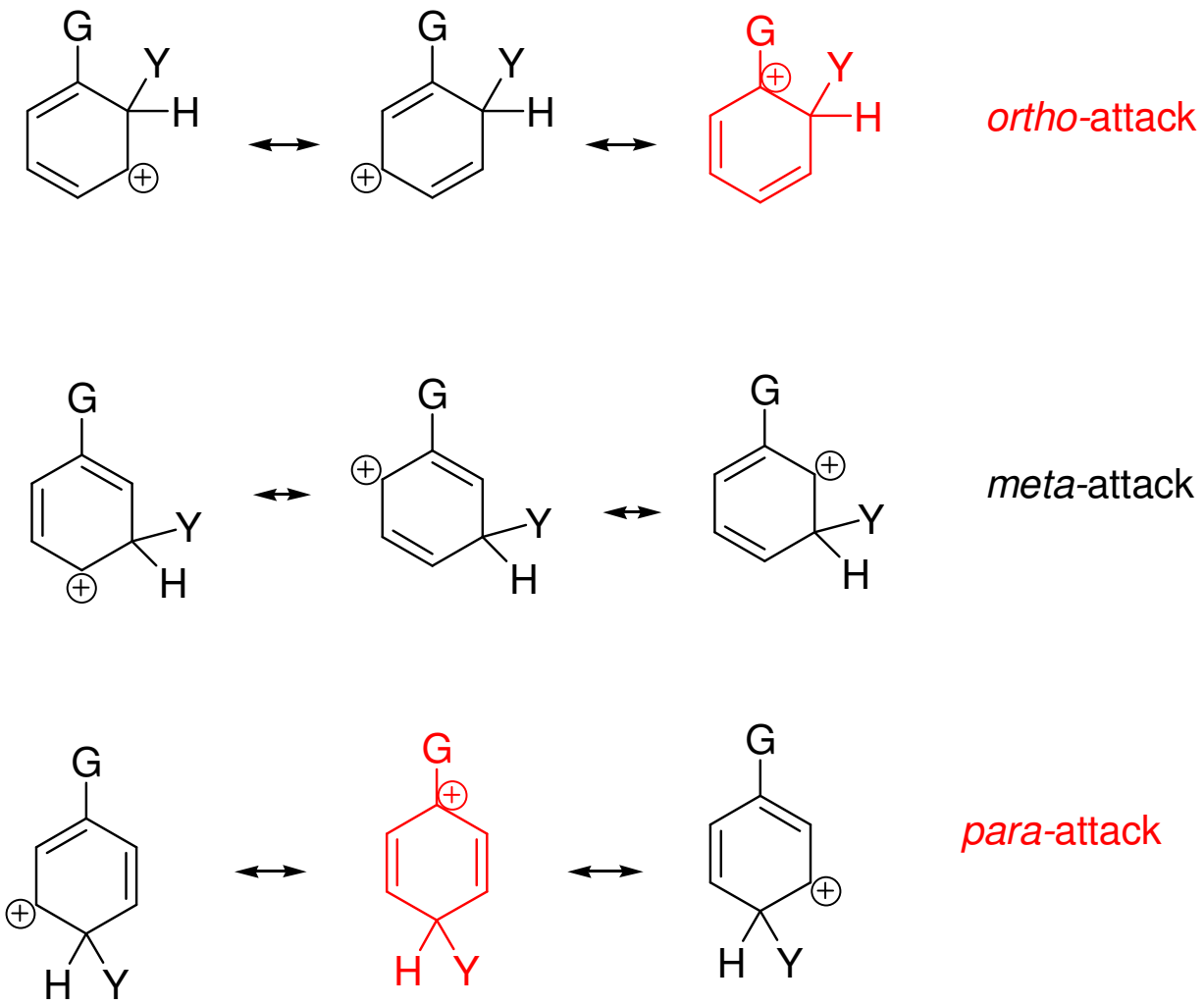

G
Y
H
ortho-attack
meta-attack
para-attack

Electron donating groups stabilize the intermediate carbocations for *ortho-* and *para-* in EAS more than for *meta-*. The Eact's for *ortho-/para-* are lower and the rates are faster.

Electron donating groups direct *ortho-/para-* in EAS



If G is an electron withdrawing group, these structures are especially unstable.

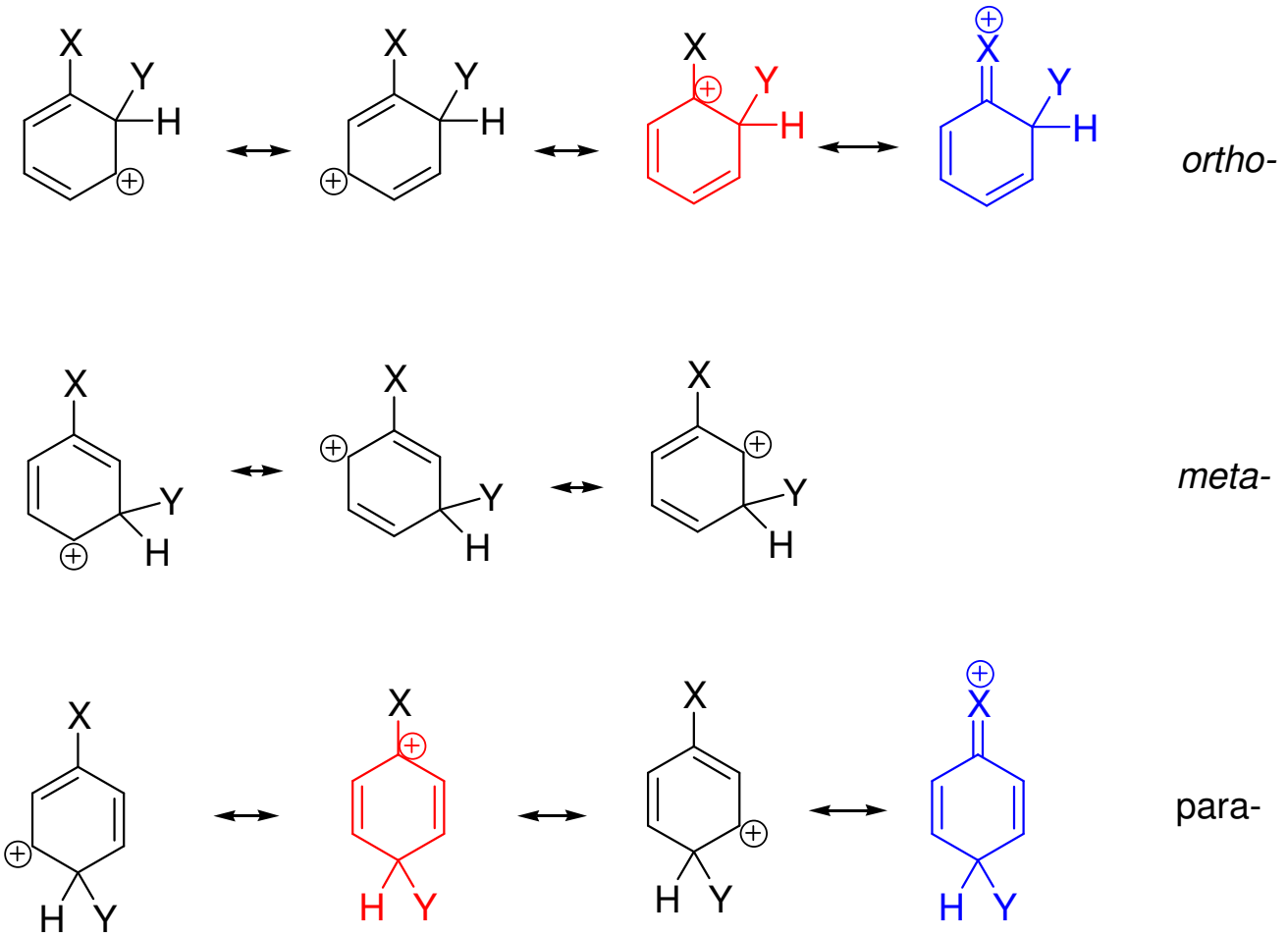

G
Y
H
ortho-attack
meta-attack
para-attack

Electron withdrawing groups destabilize the intermediate carbocations for *ortho-* and *para-* in EAS more than for *meta-*. The Eact's for *ortho-/para-* are higher and the rates are slower.

Electron withdrawing groups direct *meta-* in EAS

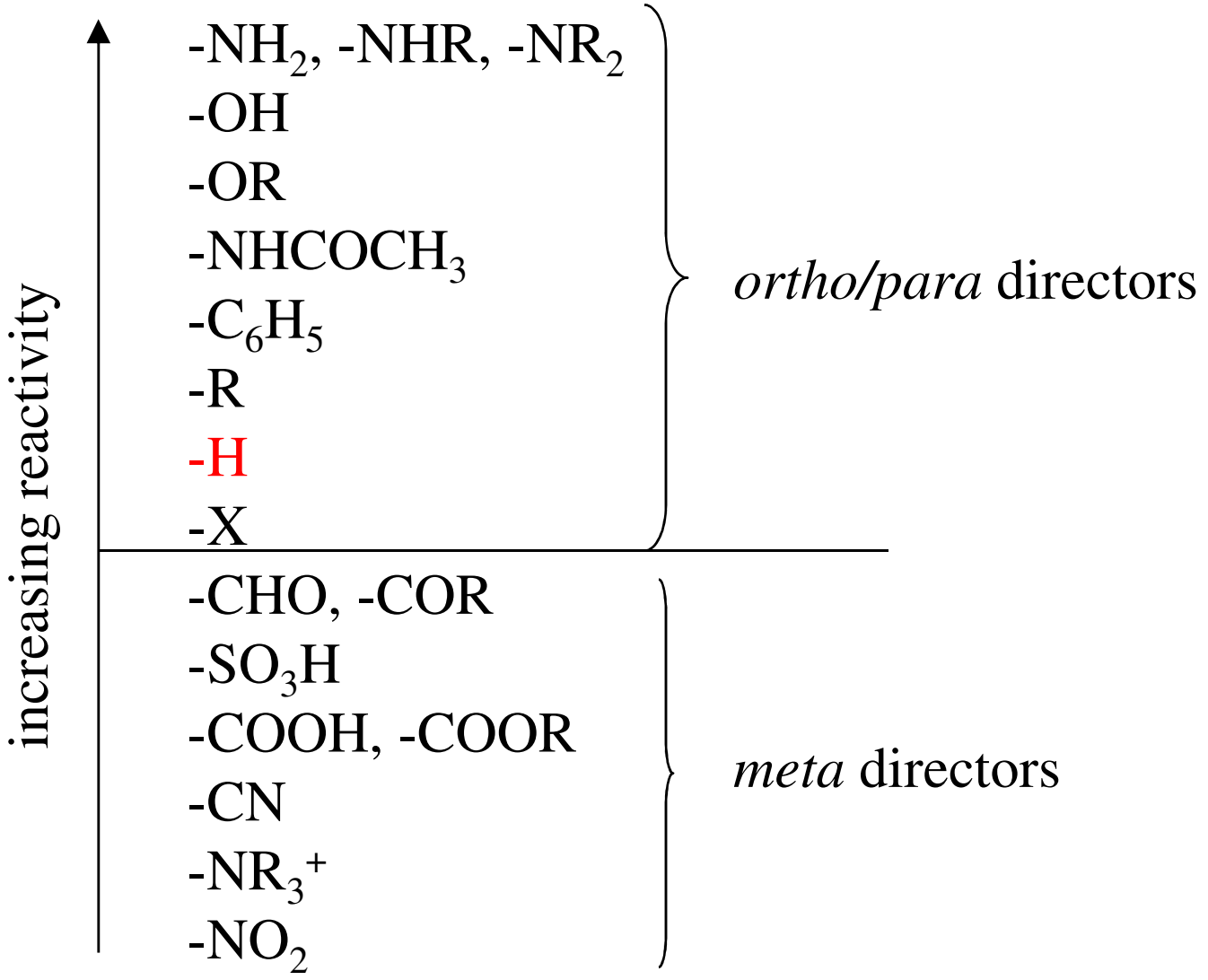
Halogens are electron withdrawing but are ortho/para directing in EAS.

The halogen atom is unusual in that it is highly electronegative but also has unshared pairs of electrons that can be resonance donated to the carbocation.



halogens are deactivating in EAS but direct ortho and para

Common substituent groups and their effect on EAS:



THANK YOU