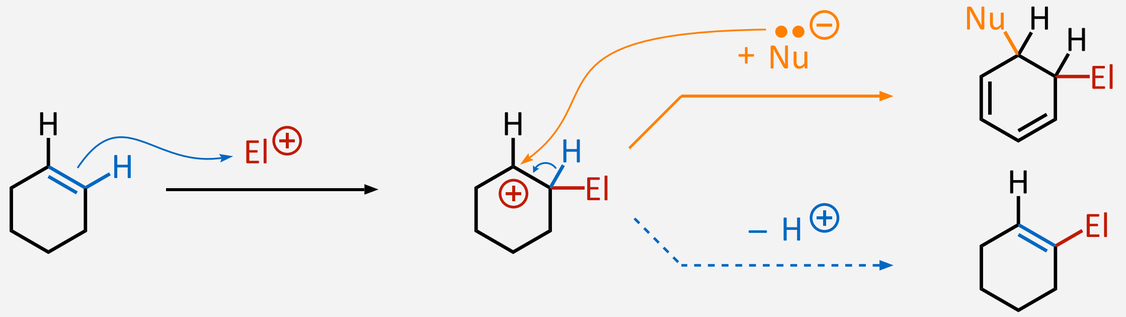
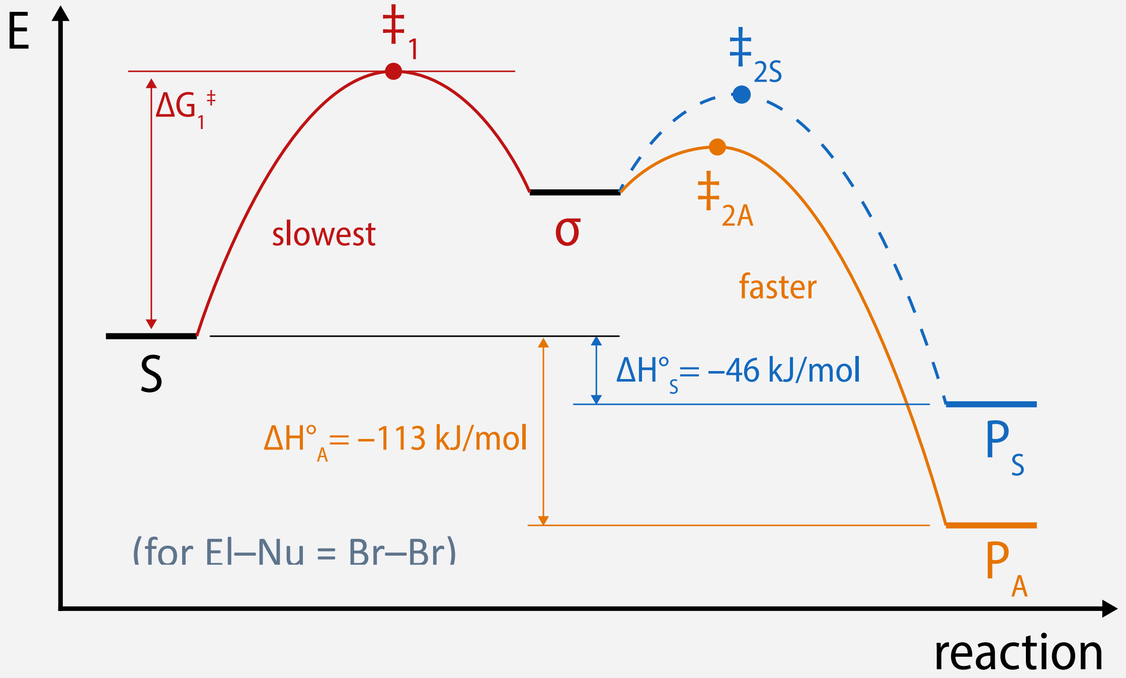
# 4.7 Electrophilic Substitutions on Aromatic Systems ($S_E$)

# Electrophilic Substitution versus Addition in Alkenes



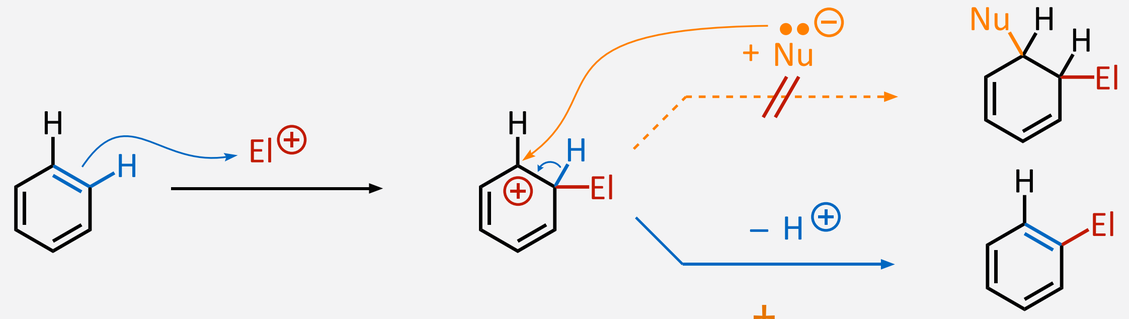

electrophilic addition

(electrophilic substitution)



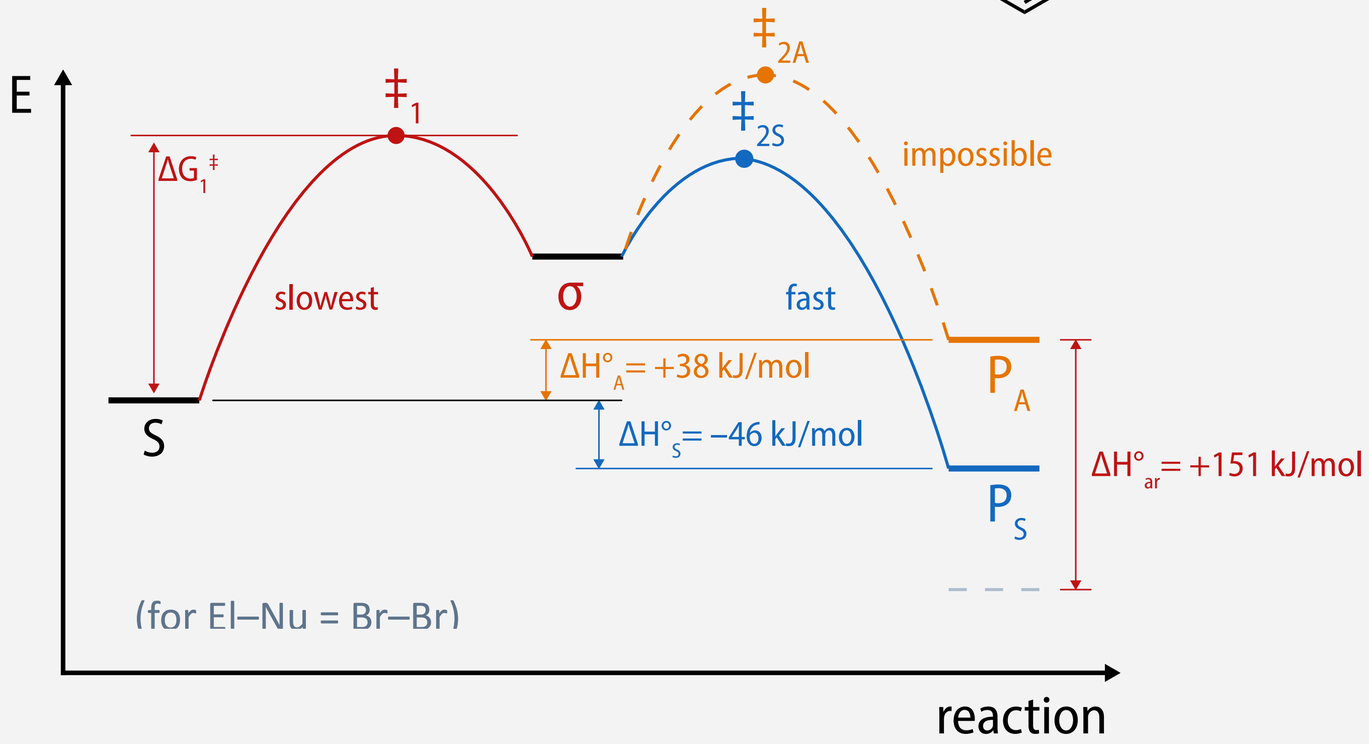

- **electrophilic substitution** to double bonds is possible but **less favorable** than **electrophilic addition**

# Electrophilic Substitution versus Addition in Arenes



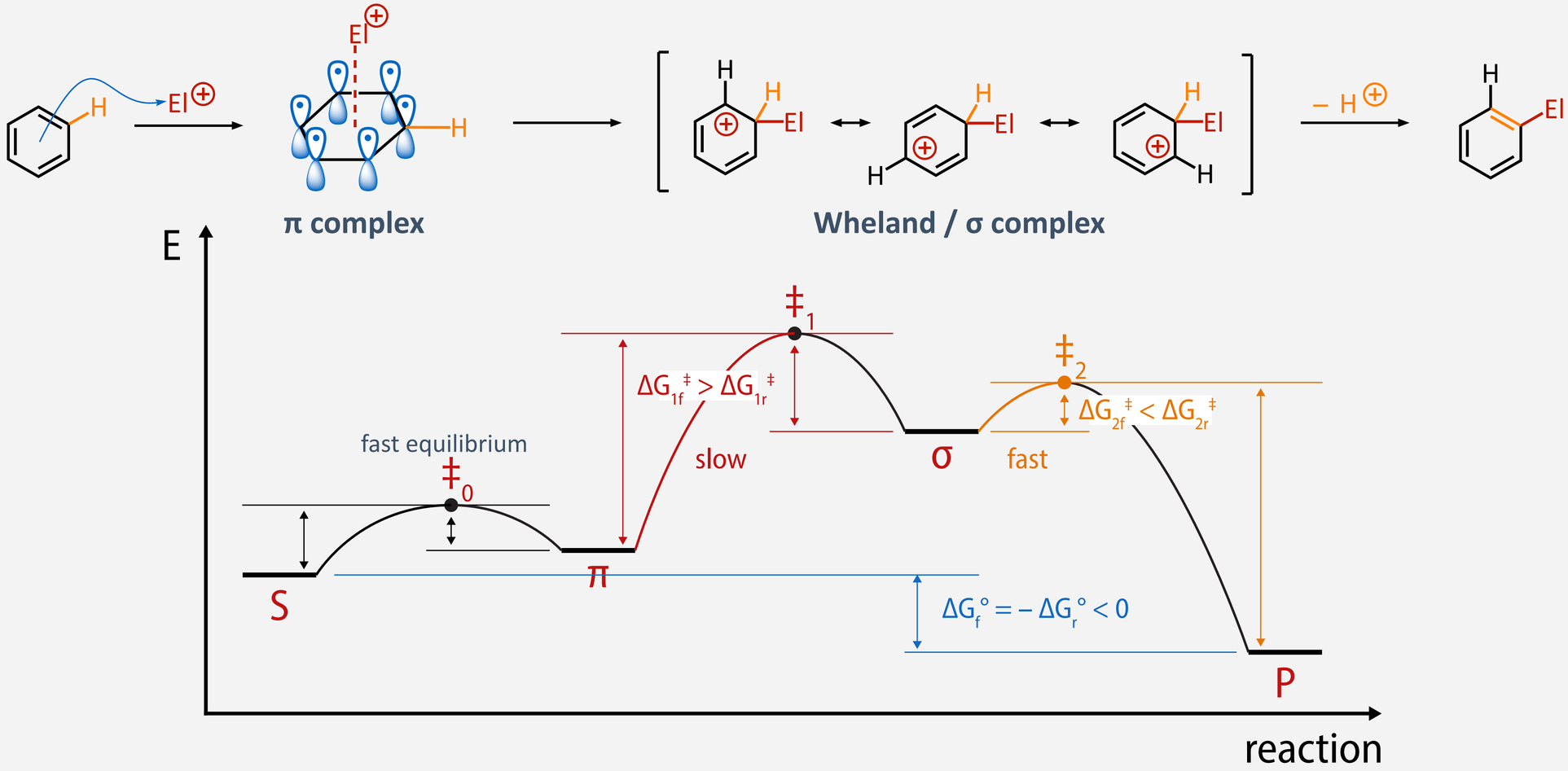

~~electrophilic addition~~

**electrophilic substitution**




- **electrophilic addition to arenes impossible because endothermic (loss of aromaticity) & exotropic**

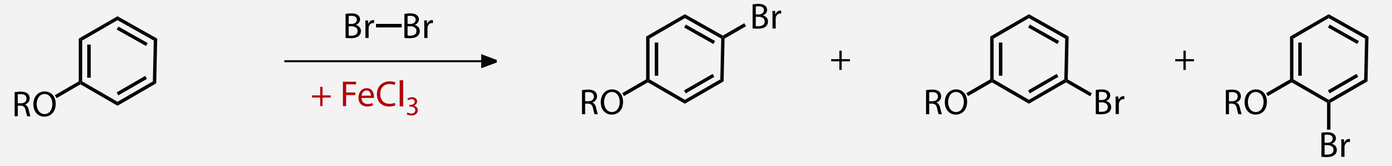
# Mechanism of Electrophilic Aromatic Substitutions ($S_EAr$)




- fast equilbrium with π complex allows electrophile to find most favorable reaction path
- electrophilic substitution is regioselective because “most acidic” proton is preferentially replaced

# Regioselectivity in Electrophilic Aromatic Substitutions

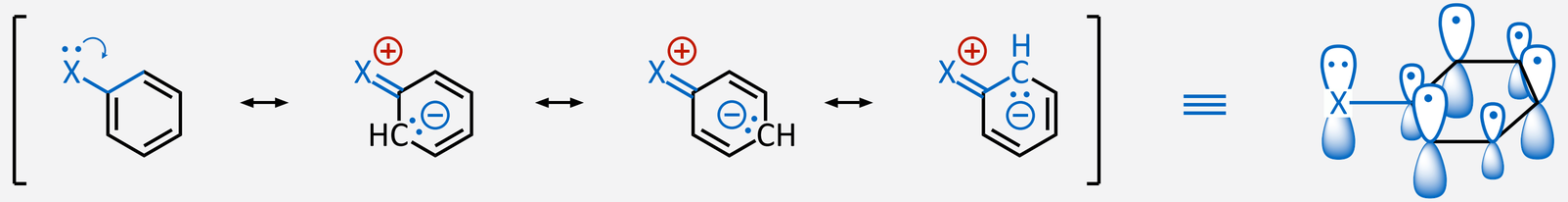
- +M substituents (heteroatoms with lone pairs, π systems) activate arenes for electrophilic substitution

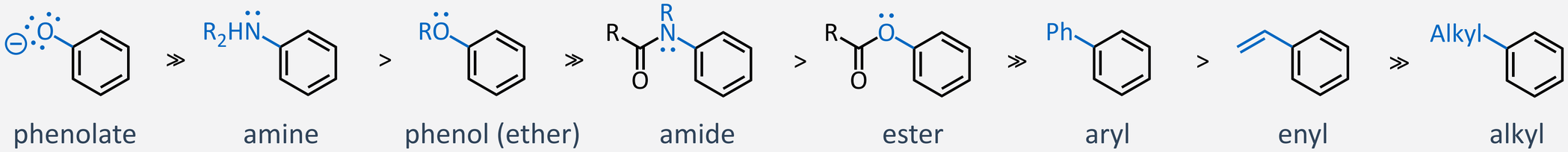



**para**
**major**

**meta**
**none**

**ortho**
**minor**



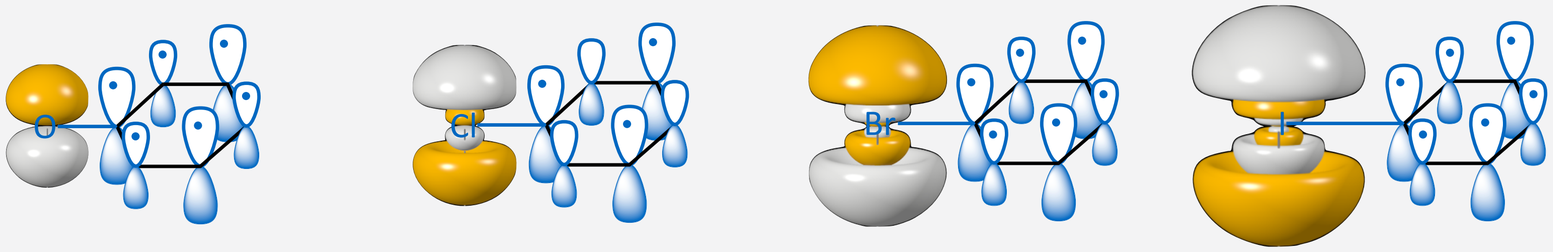




phenolate ≫ amine > phenol (ether) ≫ amide > ester ≫ aryl > enyl ≫ alkyl

- **+M (and +I) substituents increase π-electron density, stability of Wheland complex, and reactivity !**
- **+M (and +I) substituents direct the electrophile mostly into *para* (and also *ortho*) positions**

# Regioselectivity in Electrophilic Aromatic Substitutions

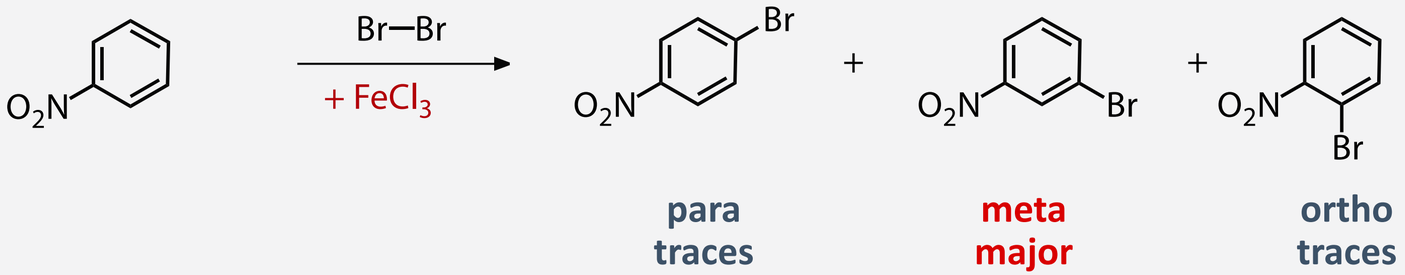
- halogens (Br, Cl, I) are –I substituents (high electronegativity) and weak +M substituents (lone pair)
- different from 2nd period elements (O, N), interaction with lone pair in 3p, 4p, 5p AO is inefficient
  - higher period p orbitals become larger and more diffuse, disadvantageous for overlap with 2p AO
  - additional node planes make for partial compensation of constructive with destructive interactions

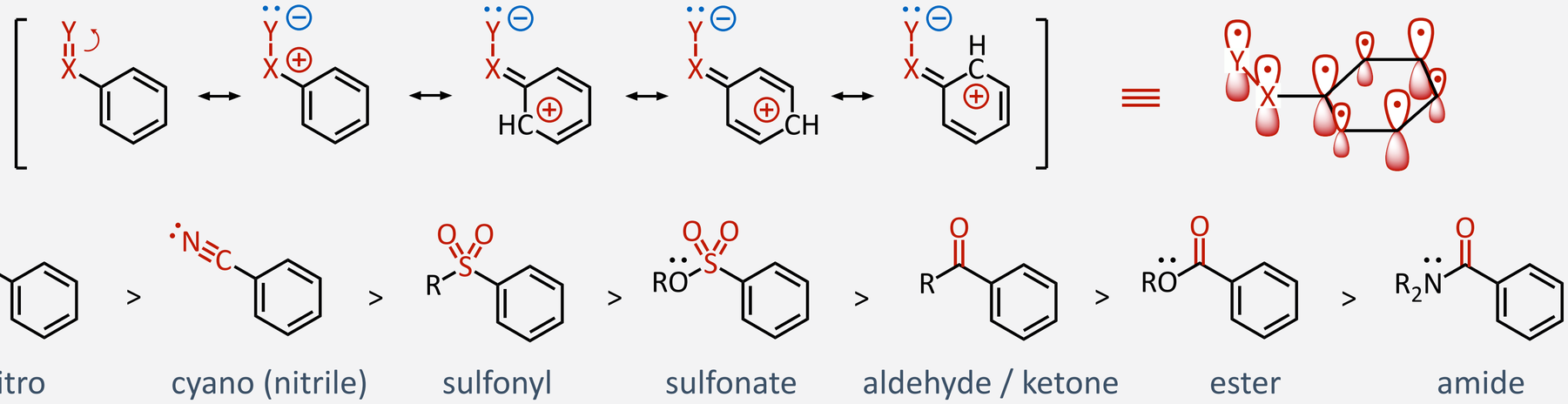



- **–I effect due to high electronegativity is not compensated anymore by +M effect (Cl > Br > I)**
- **halogens reduce π-electron density and deactivate arenes for electrophilic substitution (Cl > Br > I)**
- **nevertheless, +M effect creates a reactivity pattern (Cl > Br > I)**
- **halogens direct the electrophile mostly into *para* (and also *ortho*) positions (Cl > Br > I)**

# Regioselectivity in Electrophilic Aromatic Substitutions

- –M substituents (X=Y multiple bonds, electronegative Y) deactivate arenes for electrophilic substitution



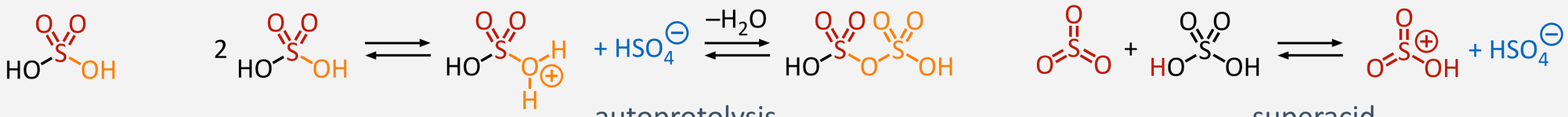




- **–M substituents decrease π-electron density, stability of Wheland complex, and reactivity !**
- **–M substituents direct the electrophile into *meta* positions**

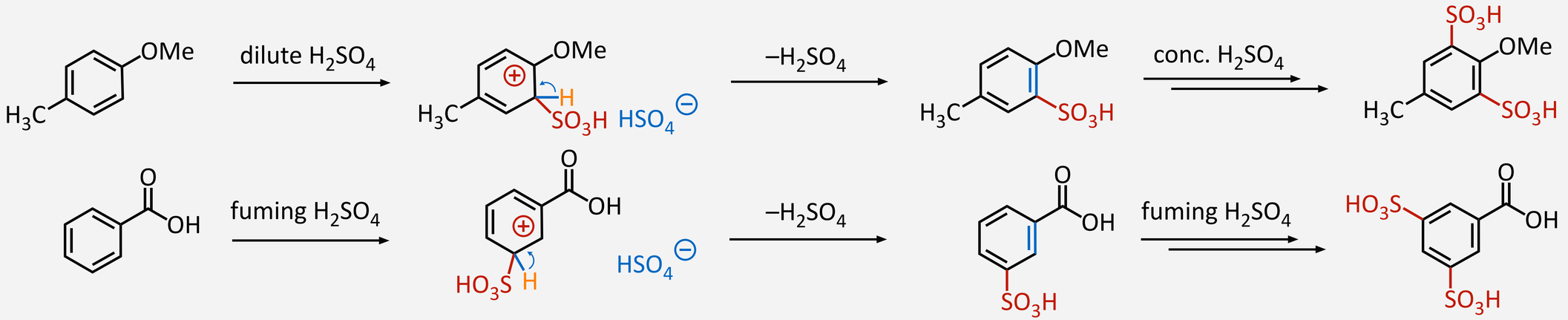
# Aryl Sulfonation

- strongly/moderately activated arenes can be sulfonated selectively with dilute/concentrated $H_2SO_4$
- deactivated arenes (and multiple sulfonation) require neat (fuming) $H_2SO_4$

**dilute $H_2SO_4$** | **concentrated $H_2SO_4$** | **neat (fuming) $H_2SO_4$**




electrophilicity

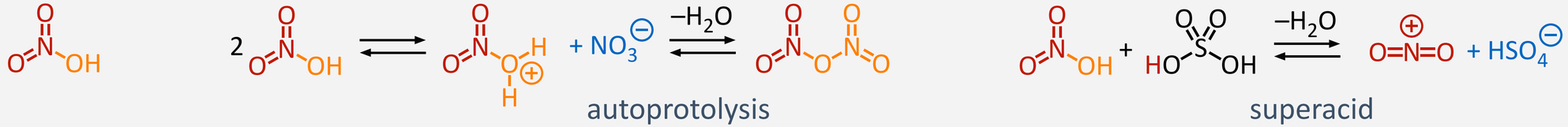



- **sulfonation deactivates arene; hence over-substitution of activated arenes not a problem !**
- **however, multiple halogenation of deactivated arenes in fuming $H_2SO_4$ is inevitable !**

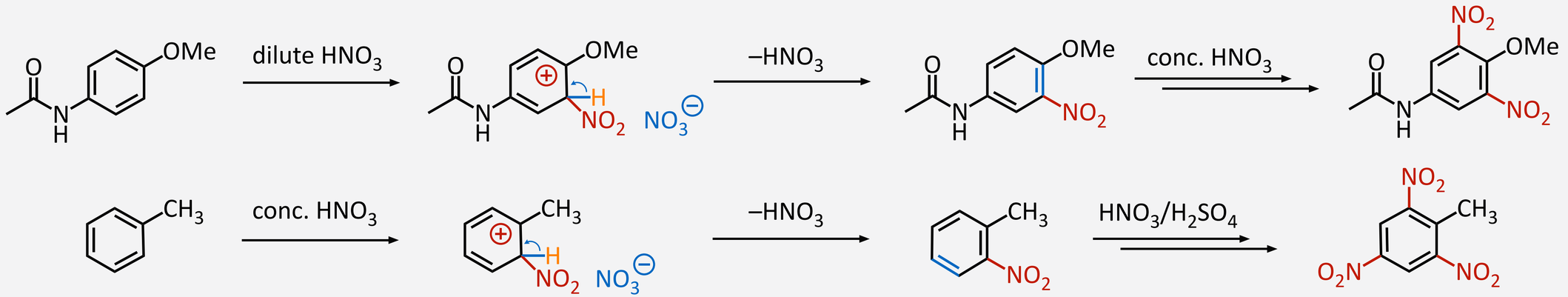
# Aryl Nitration

- strongly/moderately activated arenes can be sulfonated selectively with dilute/concentrated $HNO_3$
- deactivated arenes (and multiple sulfonation) require “nitrating acid” $HNO_3/H_2SO_4$ (2:1–1:2)

**dilute $HNO_3$** **concentrated $HNO_3$** **nitrating acid $HNO_3/H_2SO_4$**



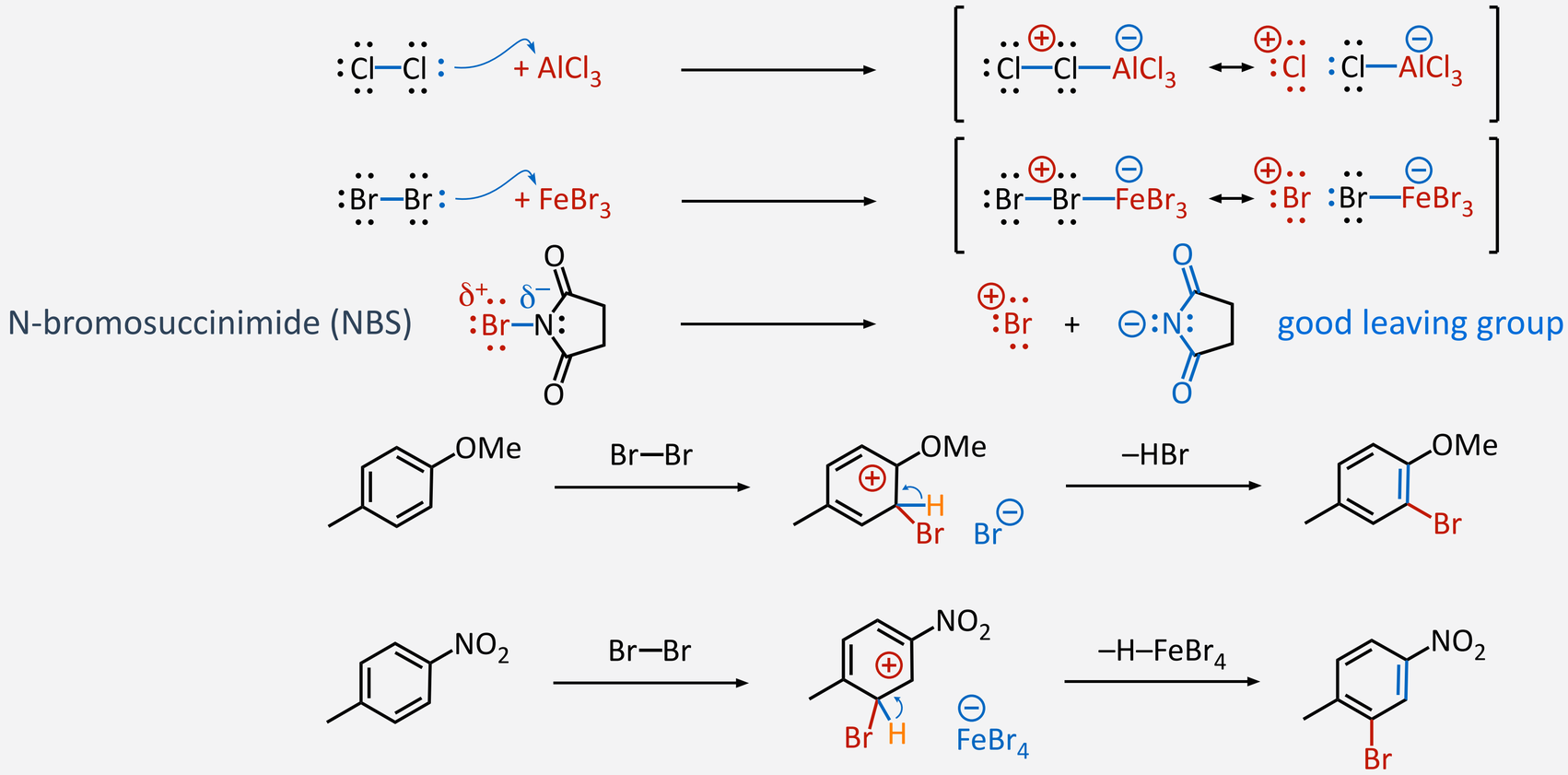

electrophilicity




- **nitration deactivates arene; hence over-substitution of activated arenes not a problem !**
- **however, multiple halogenation of deactivated arenes in nitrating acid is inevitable !**

# Aryl Halogenation

- activated arenes react with dihalogens ($Cl_2$, $Br_2$, $I_2$) without any catalyst
- deactivated arenes (and multiple halogenation) require Lewis acid catalyst to generate “halonium”



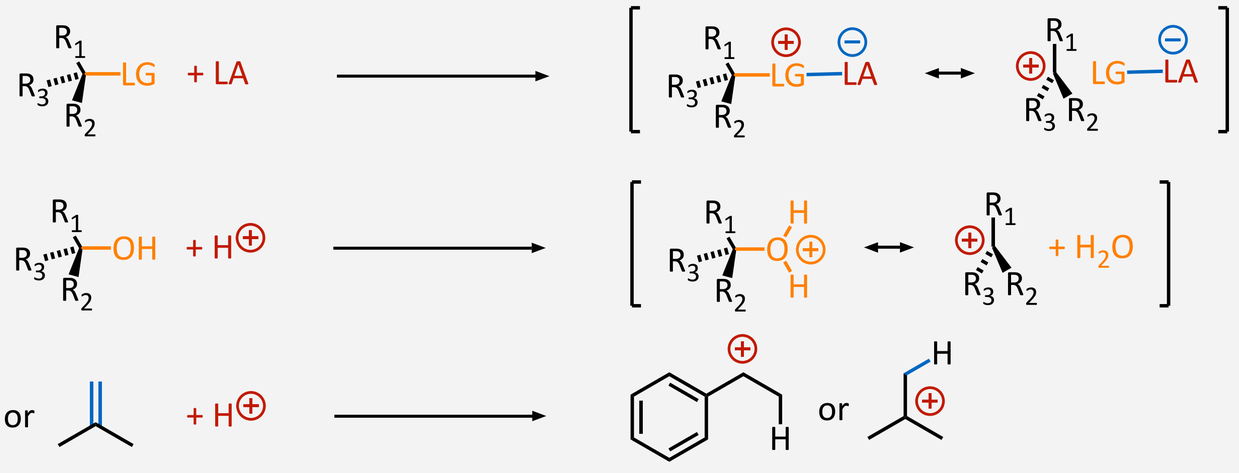

- **halogen substitution deactivates arene; product less reactive, hence over-substitution no problem !**
- **multiple halogenations can be selectively performed by simple stoichiometry control !**

# Friedel Crafts Alkylation

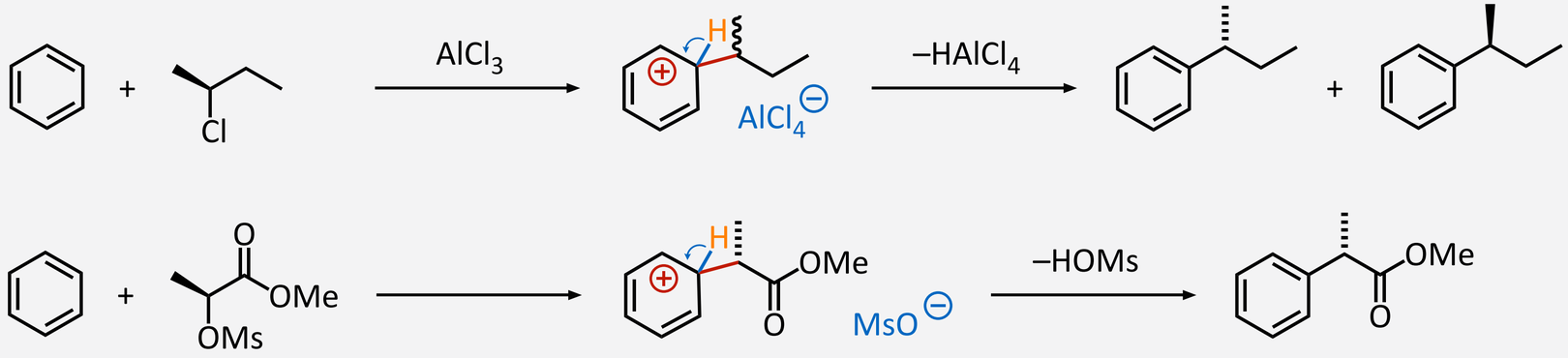
- Friedel Crafts alkylations make use of (a precursor of) a carbenium cation as the electrophile

LG = Cl, Br, I, OTs, OMs, OTf

LA = $BF_3$, $AlCl_3$, $FeBr_3$ …




- $S_EAr$ on the arene can also be looked at as $S_N1$ or $S_N2$ on the reagent with the arene as a nucleophile



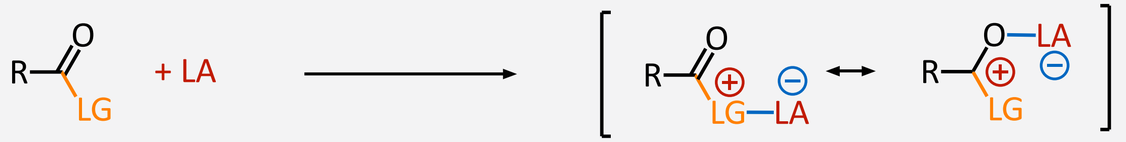

- **since alkylation (slightly) activates the resulting arene product, over-substitution is always a risk**

# Friedel Crafts Acylation

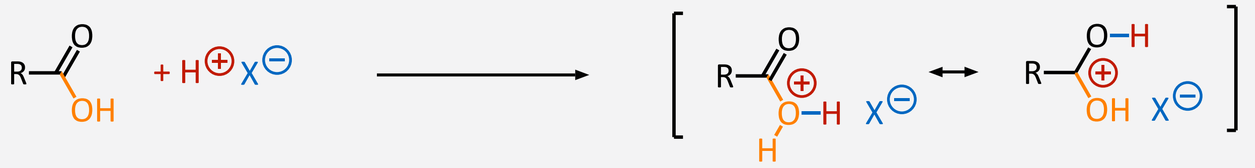
- Friedel Crafts acylations use carboxyl compounds, electrophilic activation with a Lewis/Brønsted acid

LG = Cl, O–C(=O)R

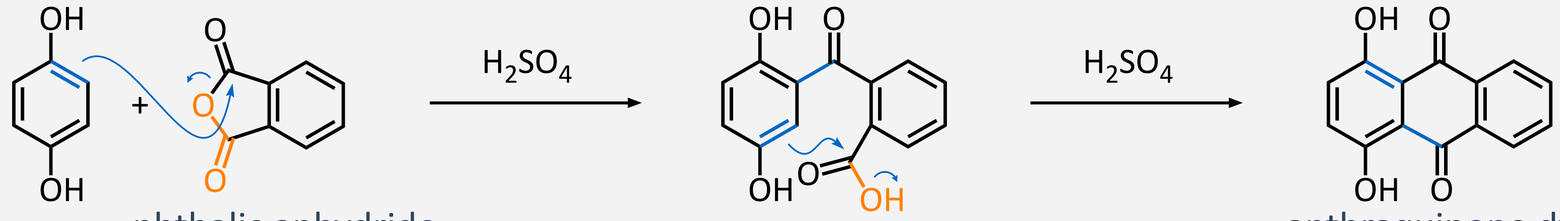
LA = $BF_3$, $AlCl_3$, $ZnCl_2$ …



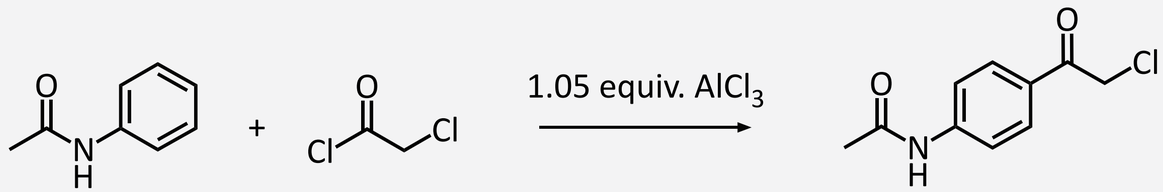

HX = $H_2SO_4$, HCl …




- $S_EAr$ on the arene can also be looked at as $S_{AE}$ on the carboxyl derivative with the arene as nucleophile



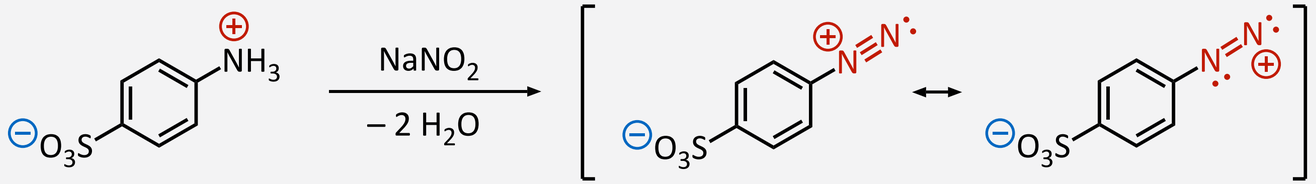

- carboxyl compounds are better electrophiles, Friedel Crafts acylations much faster than alkylations

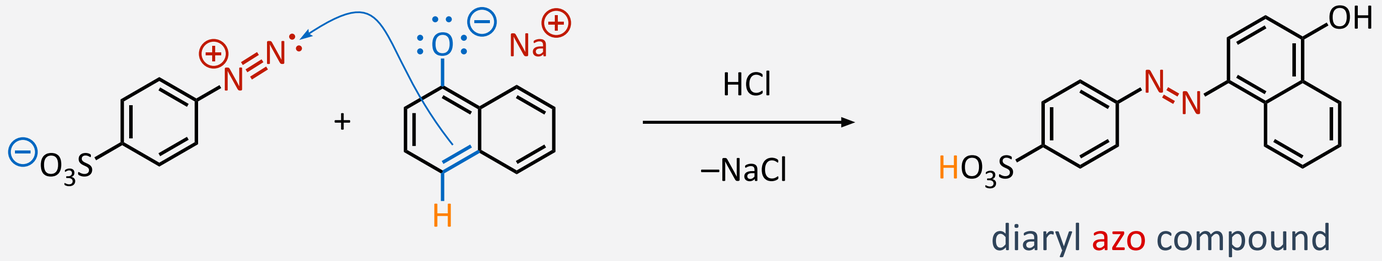



- **since acylation deactivates the arene, over-substitution is not a problem, stoichiometric control**

# Arene Diazotation

- activated arenes can be reacted with aryl diazonium compounds as weak electrophiles




- **the resulting diaryl azo compounds have a large π MO system connected via the azo function**
- **typically “push-pull” systems with a +M substituent on one side, –M substituent on the other side**
- **HOMO-LUMO gap is reduced top about 1–2 eV, high polarization, molecular dipole**
- **electron excitation on absorption of electromagnetic irradiation in the visible range (400–800 nm)**
- **azo compounds are an important class of intensely colored organic dyes**

# Learning Outcomes

- aromatic π systems are weak nucleophiles
- electrophiles add to one of the double bonds
- but subsequent nucleophile addition would result in loss of aromaticity
- instead, loss of a proton results in substitution product
- reaction is regioselective, directed by other substituents