

***Year 1 CHEM40006***  
***Reactivity at Carbon Centres***

***LECTURE 14 - Reactivity at  $sp^2$  Centres: Aromatic  
Compounds as Nucleophiles***

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# Format and scope of presentation

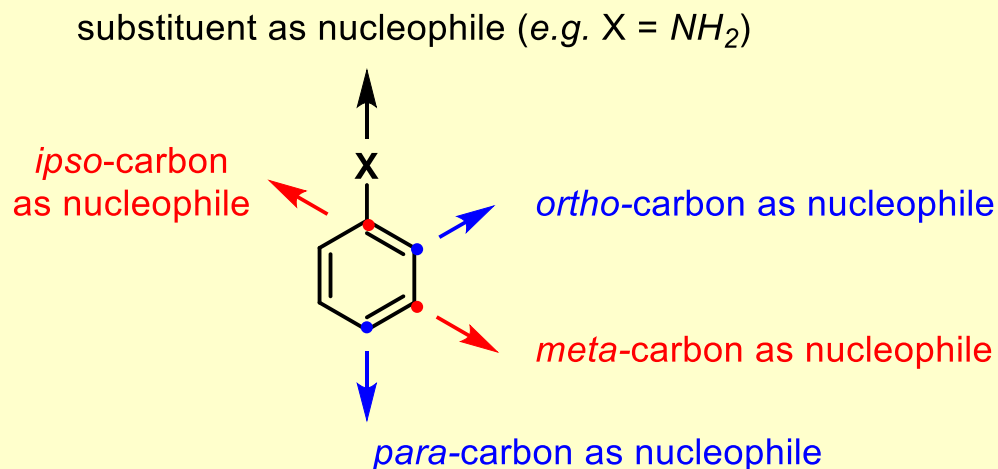
- **Electrophilic aromatic substitution ( $S_EAr$ ):**
  - Directing effects
    - *meta*-directing groups (*deactivating*)
    - *ortho/para*-directing groups which *deactivate*
    - *ortho/para*-directing groups which *activate*
    - *ortho/para*-ratios
    - *ipso*-directing groups
  - Polysubstituted aromatics
    - cooperating and competing directing influences

**Key further reading:** Clayden, Greeves & Warren, *Organic Chemistry*, 2<sup>nd</sup> Ed., Chapter 21

- *directing effects* – pages 479 - 492

# Aromatics as ambident nucleophiles – *directing effects*

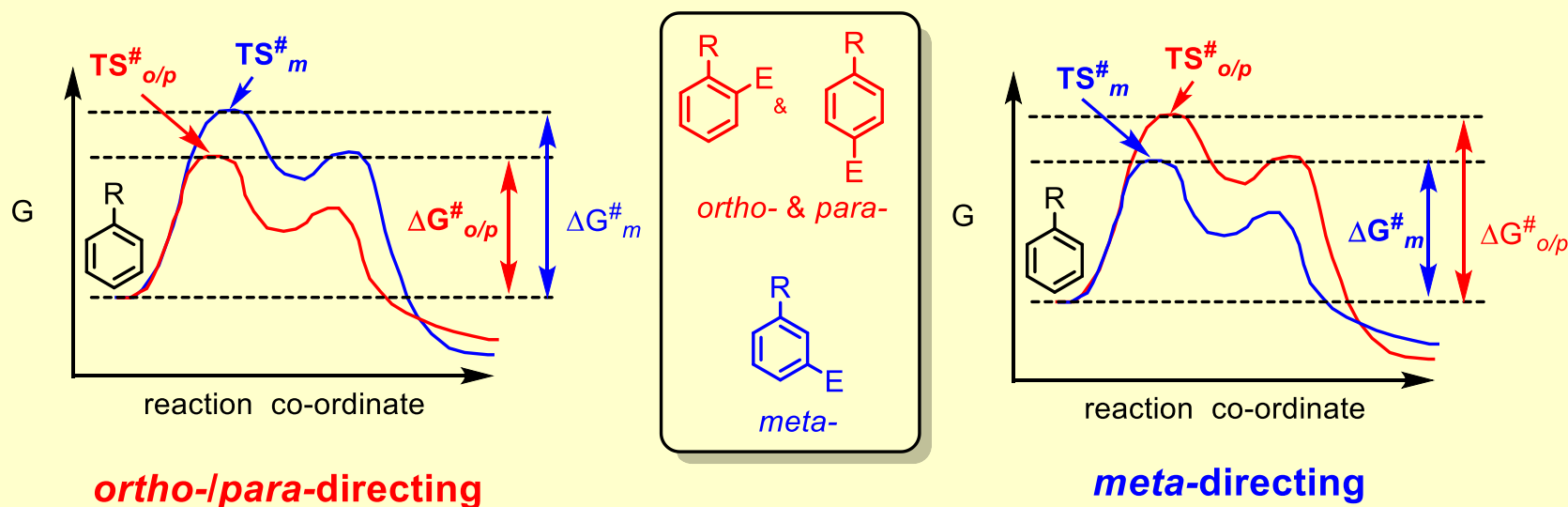
- **Substituted aromatics are ‘ambident’ nucleophiles**
  - *i.e.* they can potentially react at various positions



- **What governs the position of reactivity?**
  - The ‘directing effect’ of the substituent X
  - These fall into two broad categories:
    - *meta*-directing groups
    - *ortho/para*-directing groups...

# Directing effects

- **Electrophilic substitution is under kinetic control - i.e. fastest formed product predominates**
- **The fastest formed product will be formed via the lowest energy transition state:**

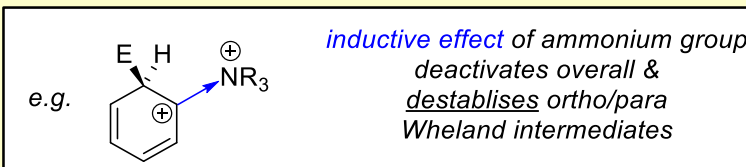


- **How can we estimate which transition state has lowest energy?**
- **HAMMONDS POSTULATE: 'energy of  $TS^{\#}$  will resemble that of Wheland intermediate more closely than the starting materials or products'**
- **We can estimate the energies of the Wheland intermediates from their resonance forms...**

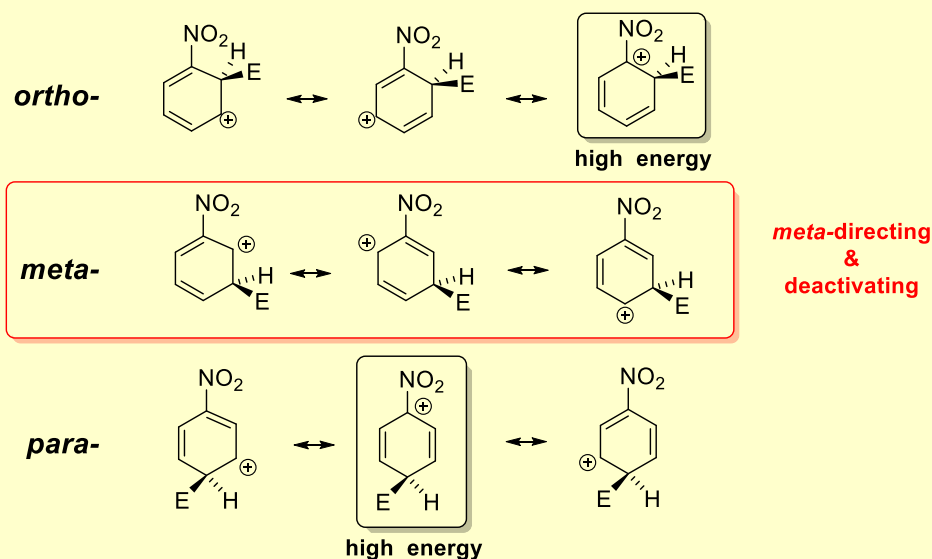
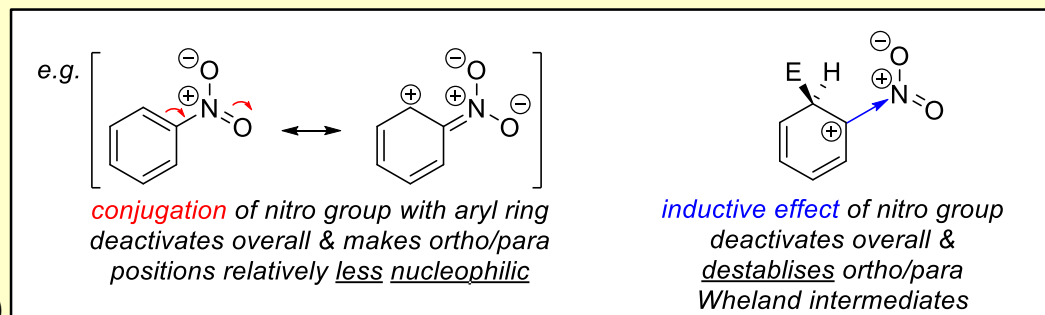
# meta-Directing groups (deactivating)

- **'Deactivated'** – i.e. less reactive than benzene (overall more electron deficient)

- **$CF_3$ ,  $NR_3^+$ ,  $NH_3^+$**   
(induction deactivates overall & destabilizes o-/p-WIs)



- **$NO_2$ ,  $CN$ ,  $SO_3H$ ,  $SO_2R$ ,  $CHO$ ,  $COR$ ,  $CO_2R$ ,  $CO_2H$**   
(conjugation deactivates overall & decreases relative reactivity of o-/p- positions;  
*induction* deactivates overall & destabilizes o-/p-WIs)



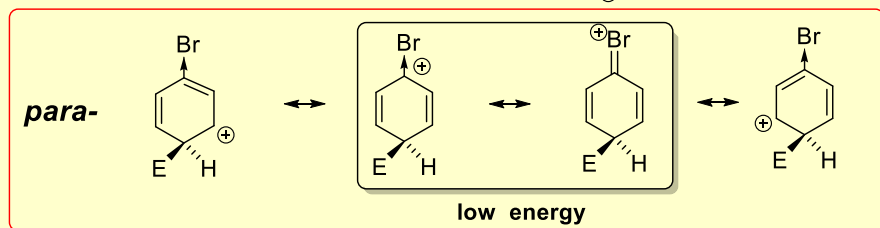
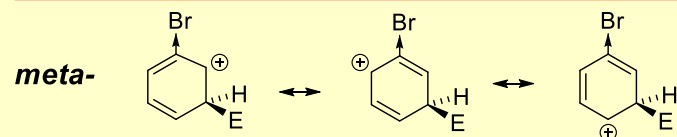
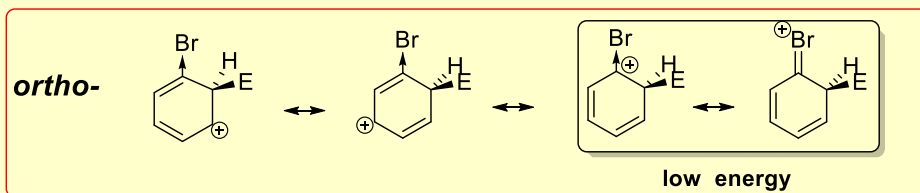
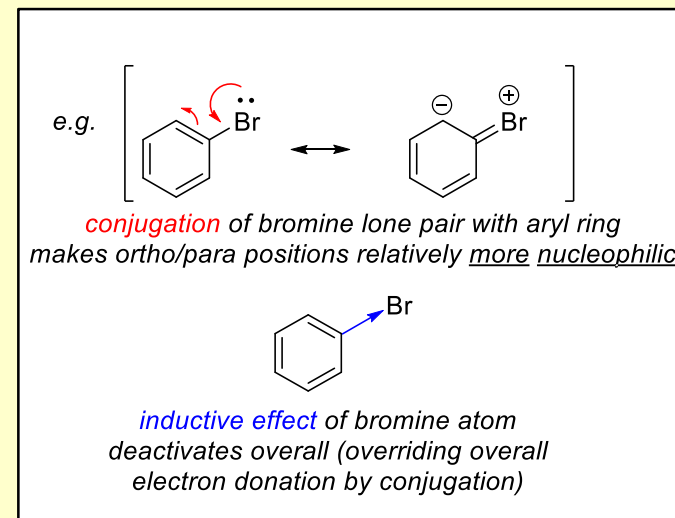
## ortho-/para-Directing (deactivating)

- **Deactivating** – i.e. less reactive than benzene (overall more electron deficient)

- **I, Br, Cl, NO**

(conjugation increases relative reactivity of o-/p- positions;  
induction deactivates overall)

i.e. conjugation dominates relative reactivity of o-/p- vs. m-  
but induction deactivates overall

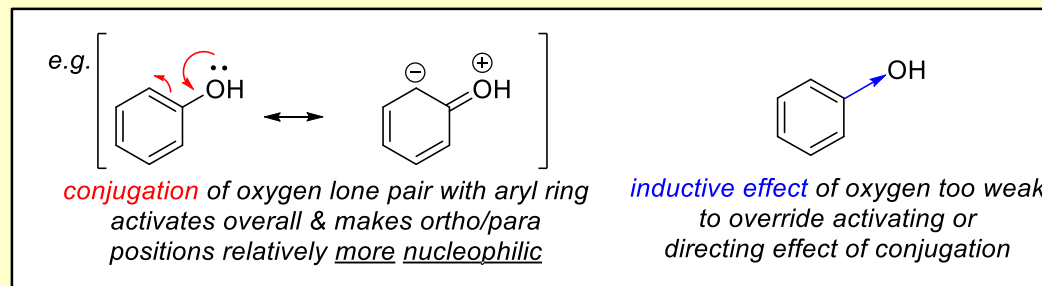


ortho-/para-directing  
&  
overall deactivating  
(induction  
outweighs  
resonance)

# ortho-/para-Directing (activating)

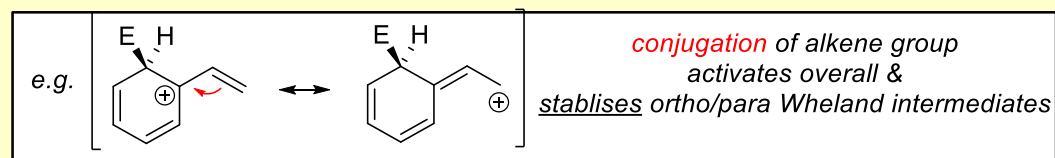
- **Activating** – i.e. more reactive than benzene (overall more electron rich)

- **$NR_2$ ,  $NH_2$ ,  $OH$ ,  $OR$ ,  $NHCOR$ ,  $OCOR$**   
(conjugation activates overall & increases relative reactivity of o-/p- positions)



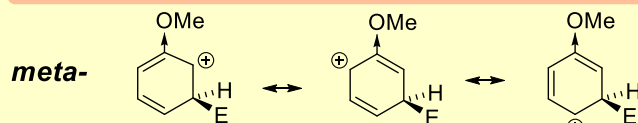
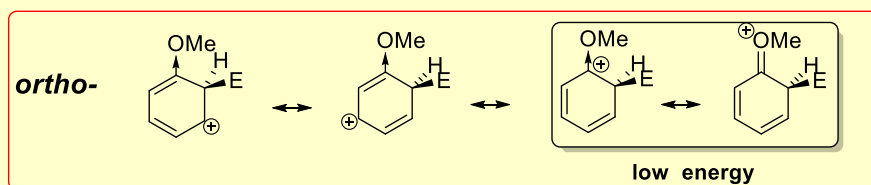
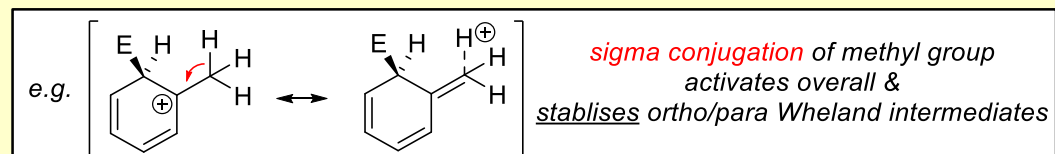
- **Alkenyl, aryl**

(conjugation activates overall & stabilizes o-/p-WIs)

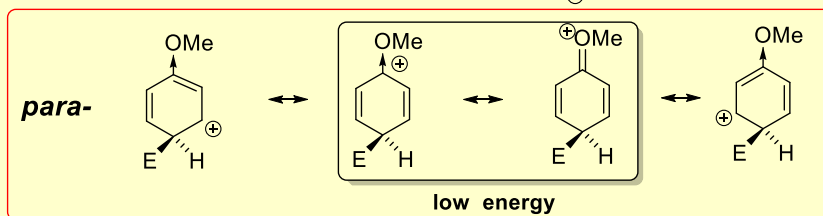


- **Alkyl**

(sigma conjugation activates overall & stabilizes o-/p-WIs)

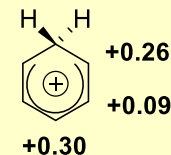


**ortho-/para-directing & overall activating (resonance outweighs induction)**

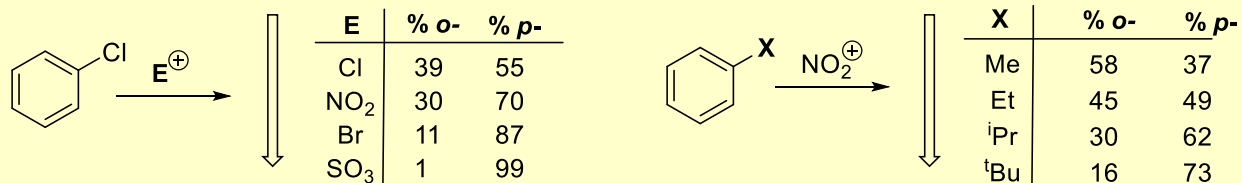


# ortho-/para-Ratios

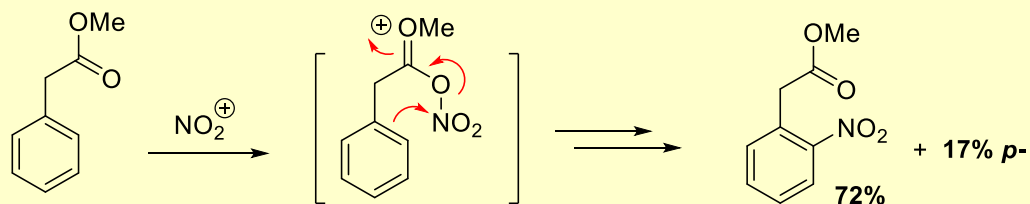
- **Statistically we expect ~2:1 ortho- : para-**
- **Theoretical charge density studies favour the para-**



- **Steric effects (large  $E^+$  or directing substituent or both) disfavour the ortho-**



- **Complexation (chaperone) effects can favour the ortho-**
  - Strazzolini *J. Org. Chem.* **1998**, 63, 952 ([DOI](#))

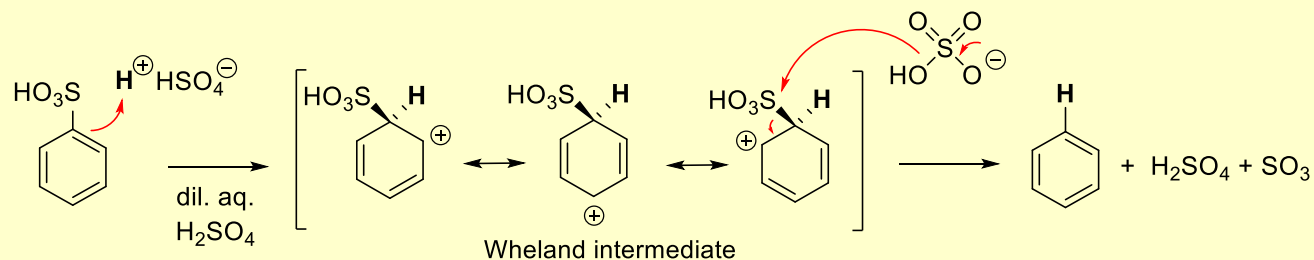


- **Solvent effects are difficult to predict**

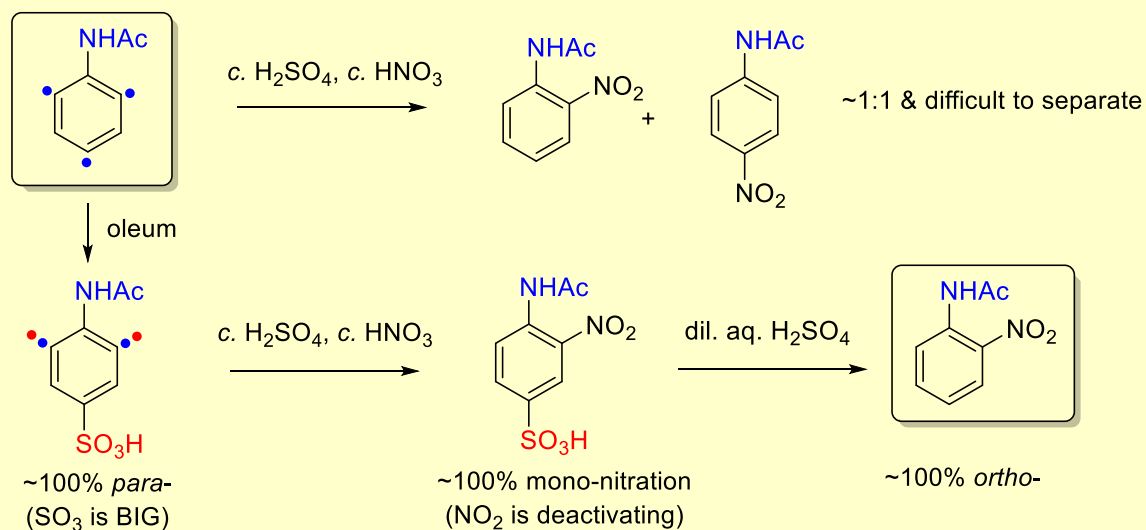


# ipso-Substitution

- Proto-desulfonylation:**

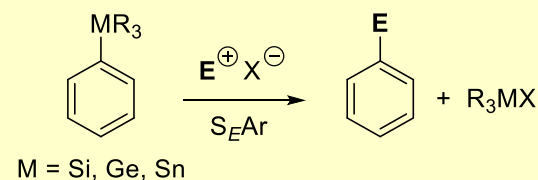


- Utility of  $\text{SO}_3\text{H}$  as temporary directing group**



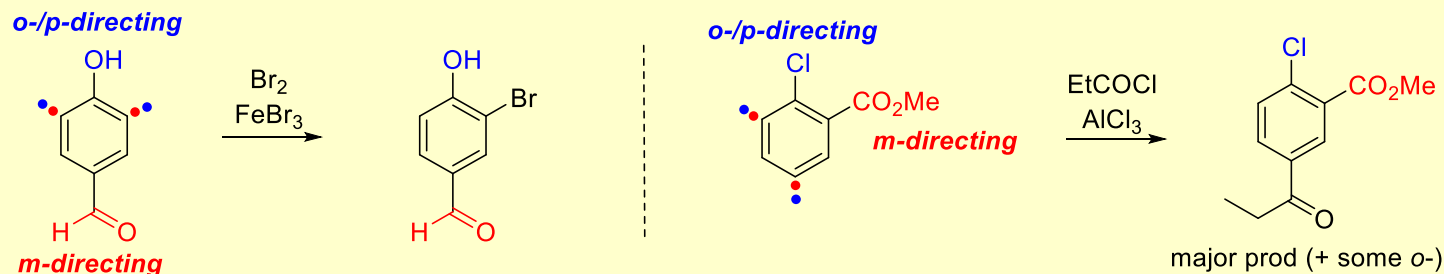
- Desilylation, degermylation & destannylation:**

– **Review:** Eaborn *J. Organometal. Chem.* **1975**, 100, 43 ([DOI](#))



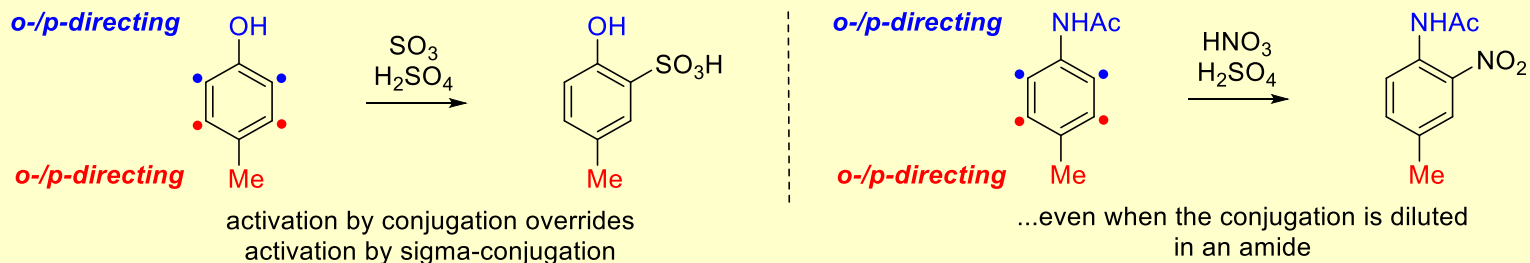
# Polysubstituted Aromatics

- Two substituents direct to the same positions - cooperation:

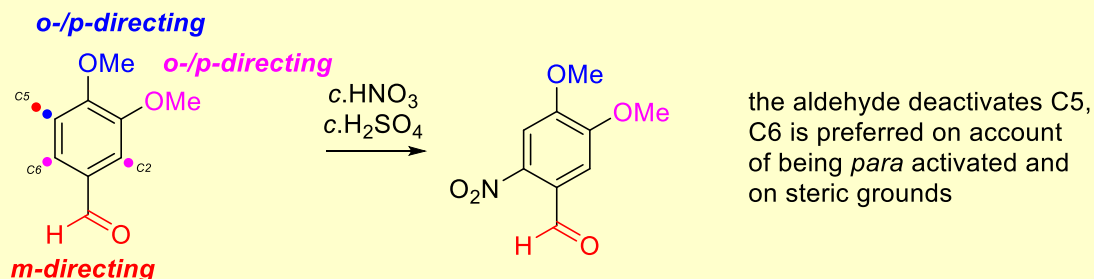


- Two substituents activate different positions – competition:

- two activating groups – the more powerful director dominates:



- an activating & a deactivating group: in general, activating effects override deactivating effects:



## Synthetic 'check list' for $S_EAr$

- ***Will  $E^+$  react at ring carbon or elsewhere (e.g. at amine substituent -> diazonium salt)?***
- ***Is the  $E^+$  sufficiently reactive to react with a ring carbon?***
- ***If reaction at a ring carbon is expected, what orientation relative to existing group(s) (i.e. directing effects)?***
  - *ortho-/para- or meta- or ipso-?*
  - *If ortho-/para- ...which?*
  - *Do directing effects of existing groups cooperate or compete?*
  - *Use a temporary directing group to get desired orientation?*
- ***Mono- or multiple substitution?***
  - *Will introduction of E activate or deactivate the ring relative to the starting material?*