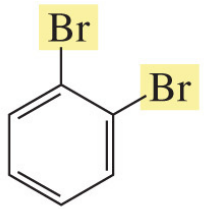
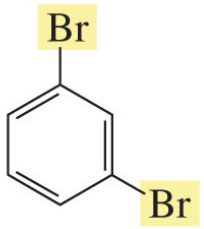
Naming di- and poly-substit'd bz

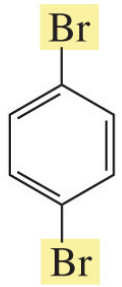
- disubstituted = 2 subs



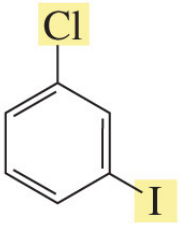
1,2-dibromobenzene
ortho-dibromobenzene
o-dibromobenzene



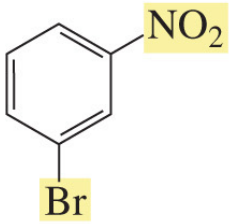
1,3-dibromobenzene
meta-dibromobenzene
m-dibromobenzene



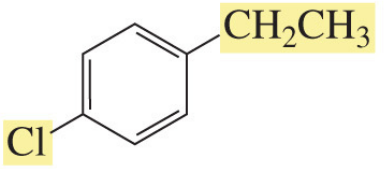
1,4-dibromobenzene
para-dibromobenzene
p-dibromobenzene



1-chloro-3-iodobenzene
meta-chloroiodobenzene
not
1-iodo-3-chlorobenzene or
meta-iodochlorobenzene



1-bromo-3-nitrobenzene
meta-bromonitrobenzene



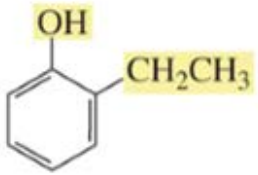
1-chloro-4-ethylbenzene
para-chloroethylbenzene

- alphabetical order
- lowest number

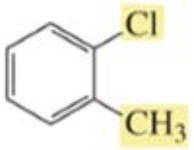
- disubstituted with own name

4-nitroaniline
para-nitroaniline

1-amino-4-nitrobenzene

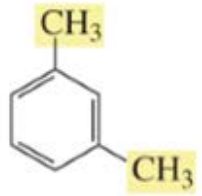


2-ethylphenol
ortho-ethylphenol



~~2-chloromethylbenzene~~
~~*ortho*-chloromethylbenzene~~

IUPAC ~ 1-chloro-2-methylbenzene
However, *o*-chlorotoluene
2-chlorotoluene quite OK



1,3-dimethylbenzene
meta-xylene

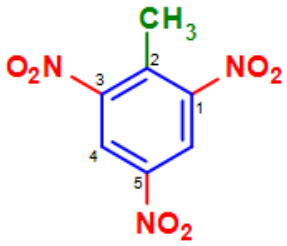


Figure 18. TNT, as named under the IUPAC nomenclature. Note that since the IUPAC nomenclature does not recognize toluene as the primary base of this compound, substituent priorities are reverted to normal defaults.
As a result, TNT in IUPAC is named (systematic name):
2-methyl-1,3,5-trinitrobenzene

1,2,3,5 < 1,2,4,6

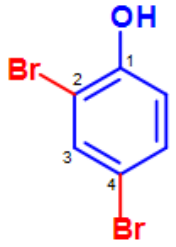
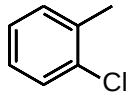


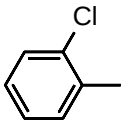
Figure 19. 2,4-dibromophenol, as shown in this diagram, is valid in both the common nomenclature as well as the IUPAC nomenclature. As mentioned previously, **phenol, benzoic acid, and benzaldehyde** substituents are allowed to be used in the IUPAC naming conventions and the base naming priority rules are applied in the nomenclature process.

Searched 'IUPAC nomenclature toluene'

2-chloromethylbenzene



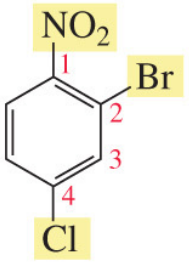
This name appears to be ambiguous



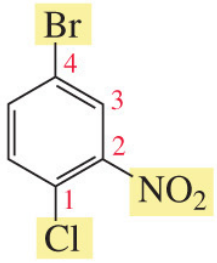
1-chloro-2-methylbenzene

ChemDraw

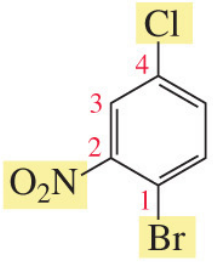
- polysubstituted



2-bromo-4-chloro-1-nitrobenzene

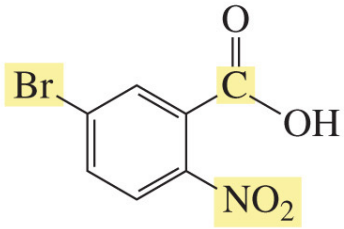


4-bromo-1-chloro-2-nitrobenzene

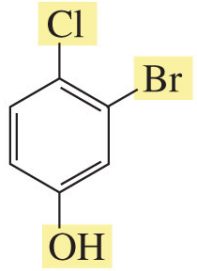


1-bromo-4-chloro-2-nitrobenzene

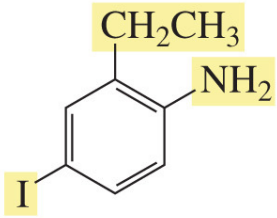
- polysubstituted with own name



5-bromo-2-nitrobenzoic acid



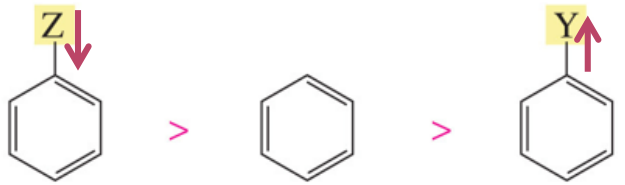
3-bromo-4-chlorophenol



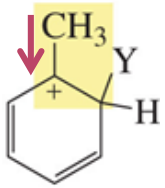
2-ethyl-4-iodoaniline

Reactions on subst'd bz

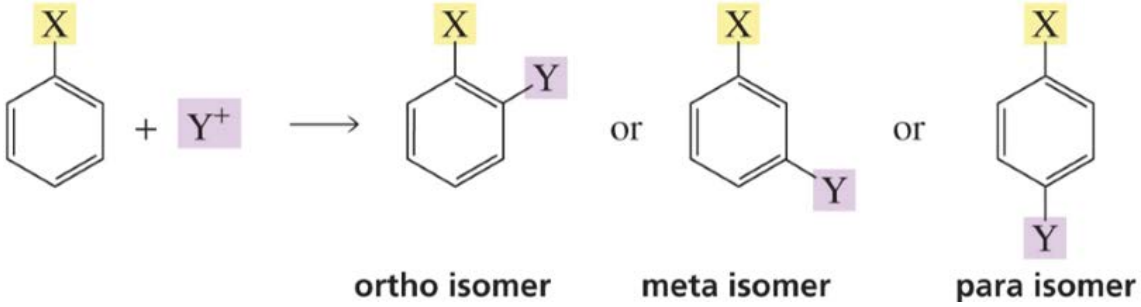
- (1st) Substituent governs reactivity and orientation (of the 2nd substitution).
- reactivity ~ activating subs or deactivating subs
  - EDG activates by
    - enhancing nucleophilicity



    - enhancing stability of C^+ interm [arenium ion] (and TS)



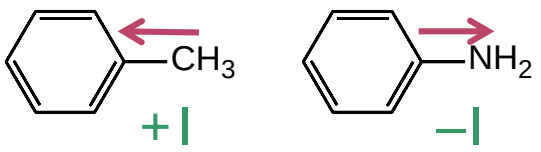
- orientation ~ ortho-para director or meta director



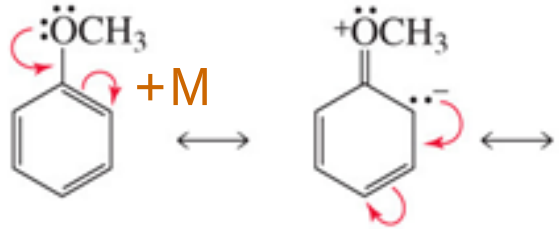
Effects of substituent

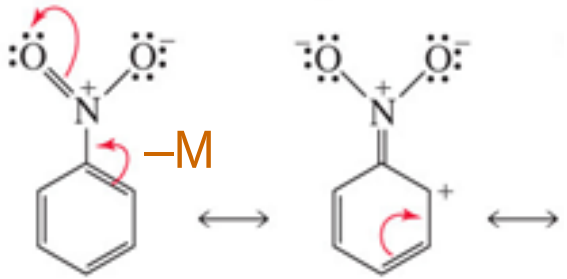
= electronic [polar] effect + steric effect See §8.10

- polar effect = inductive + resonance [mesomeric] effect
- inductive effect ~ transmission of charge thru σ bond
  - inductive ED [+I] ~ R, Ar, =, O^-
    - in this textbook, no inductive EDG
  - inductive EW [–I] ~ all others



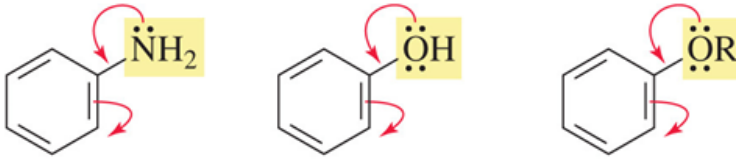
- resonance effect ~ ED or EW thru π system
  - ED by resonance [+M]
    - subs w/ : on atom directly bonded to ring
    - NH_2, OH, OR, X
  - EW by resonance [–M]
    - subs attached to ring by atom = or ≡ bonded to more EN atom
    - C=O, C≡N, SO_3H, NO_2

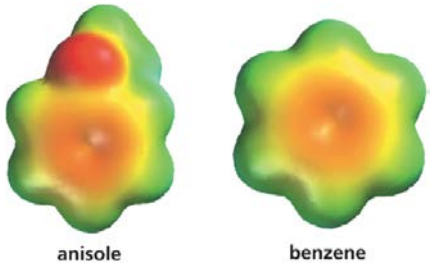




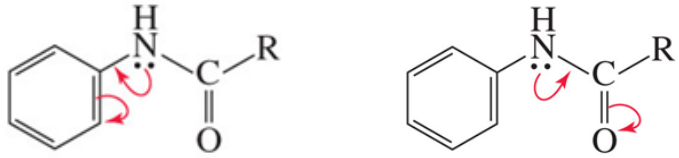
Effect of subs on reactivity

- ED subs activates [makes more reactive].
  - strongly activating subs ~ NH_2, NHR, NR_2, OH, OR
    - +M > –I

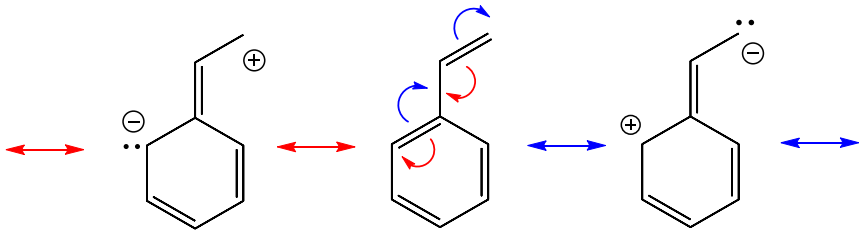




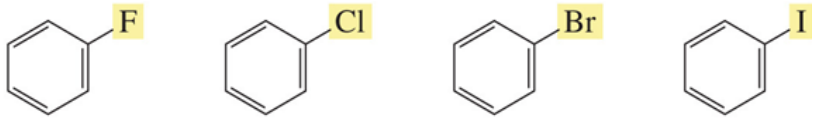
  - moderately activating subs ~ NHCOR, OCOR
    - +M > –I
    - smaller +M than SA



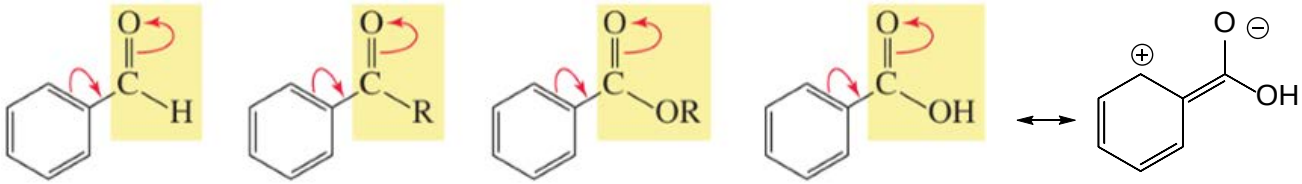
  - weakly activating subs ~ R, Ar, CH=CHR
    - (small) +I
    - in this textbook
      - R ~ ED by hyperconjugation
      - Ar and = ~ ED by +M > –M



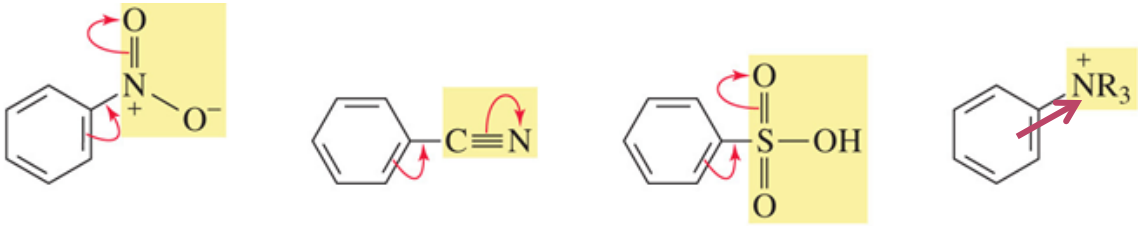
- EW subs deactivates [makes less reactive].
  - weakly deactivating subs ~ X



    - +M < –I
    - small +M for Cl, Br, I (overlap); large –I for F (EN)
  - moderately deactivating subs ~ COY, COOY
    - –M and –I



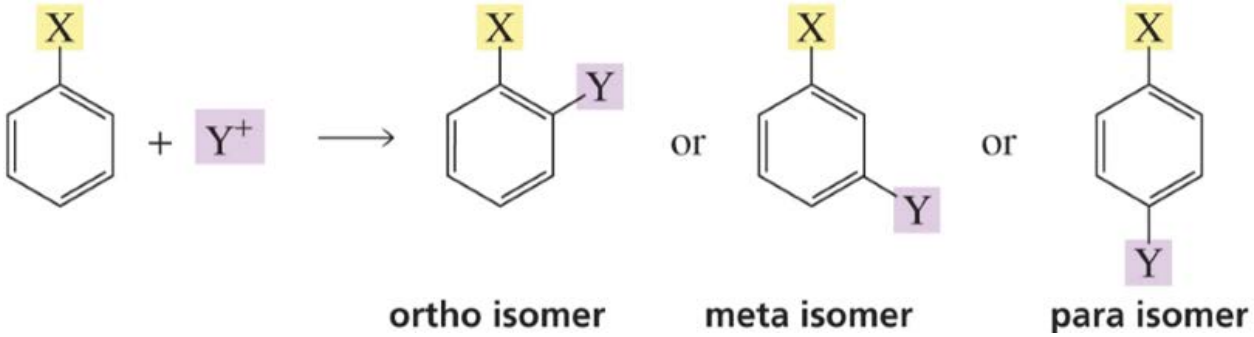
  - strongly deactivating subs ~ NO_2, CN, SO_3H, N^+
    - –M and –I



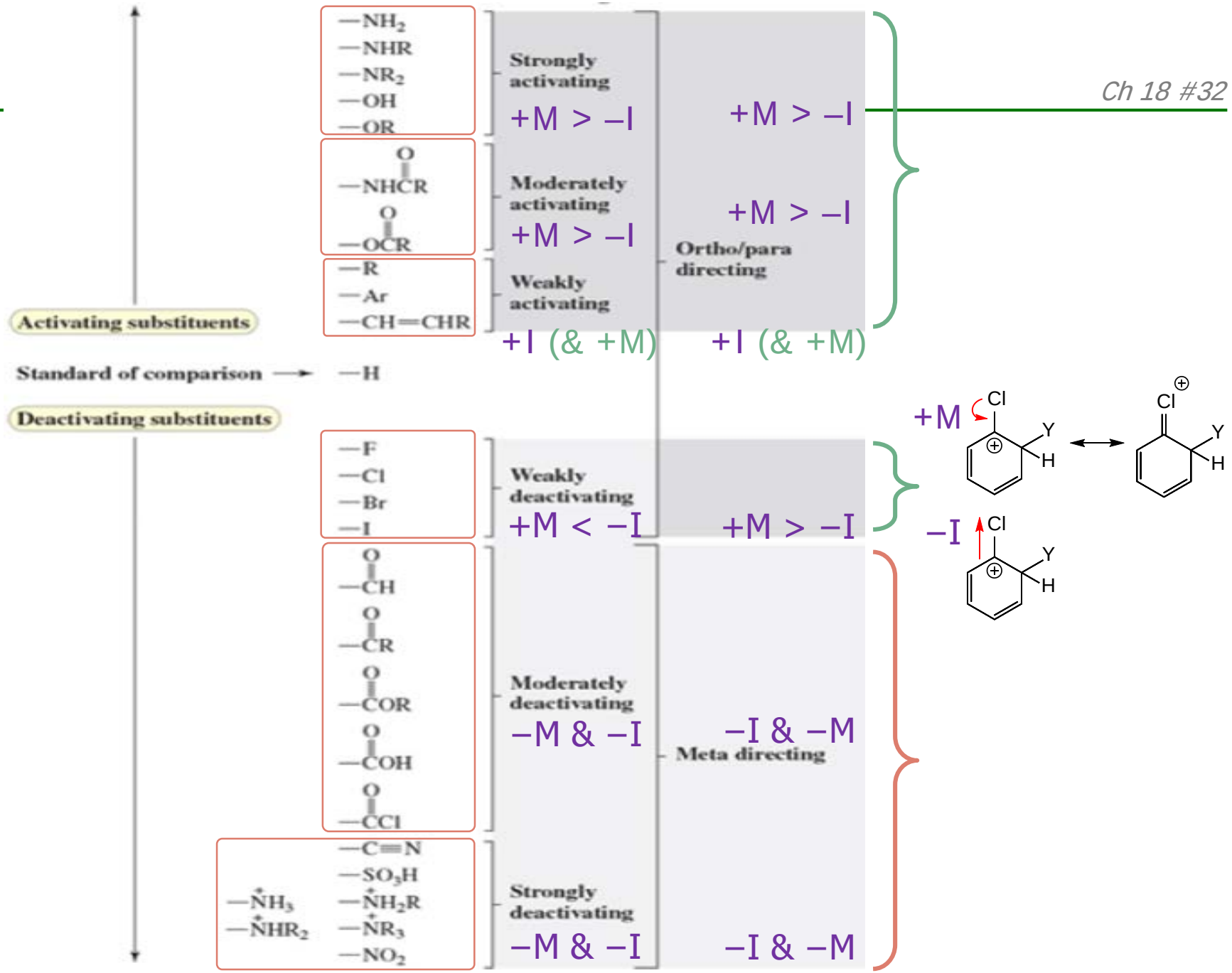
    - N^+ [ammonium] ~ no M and (large) –I

Effect of subs on orientation

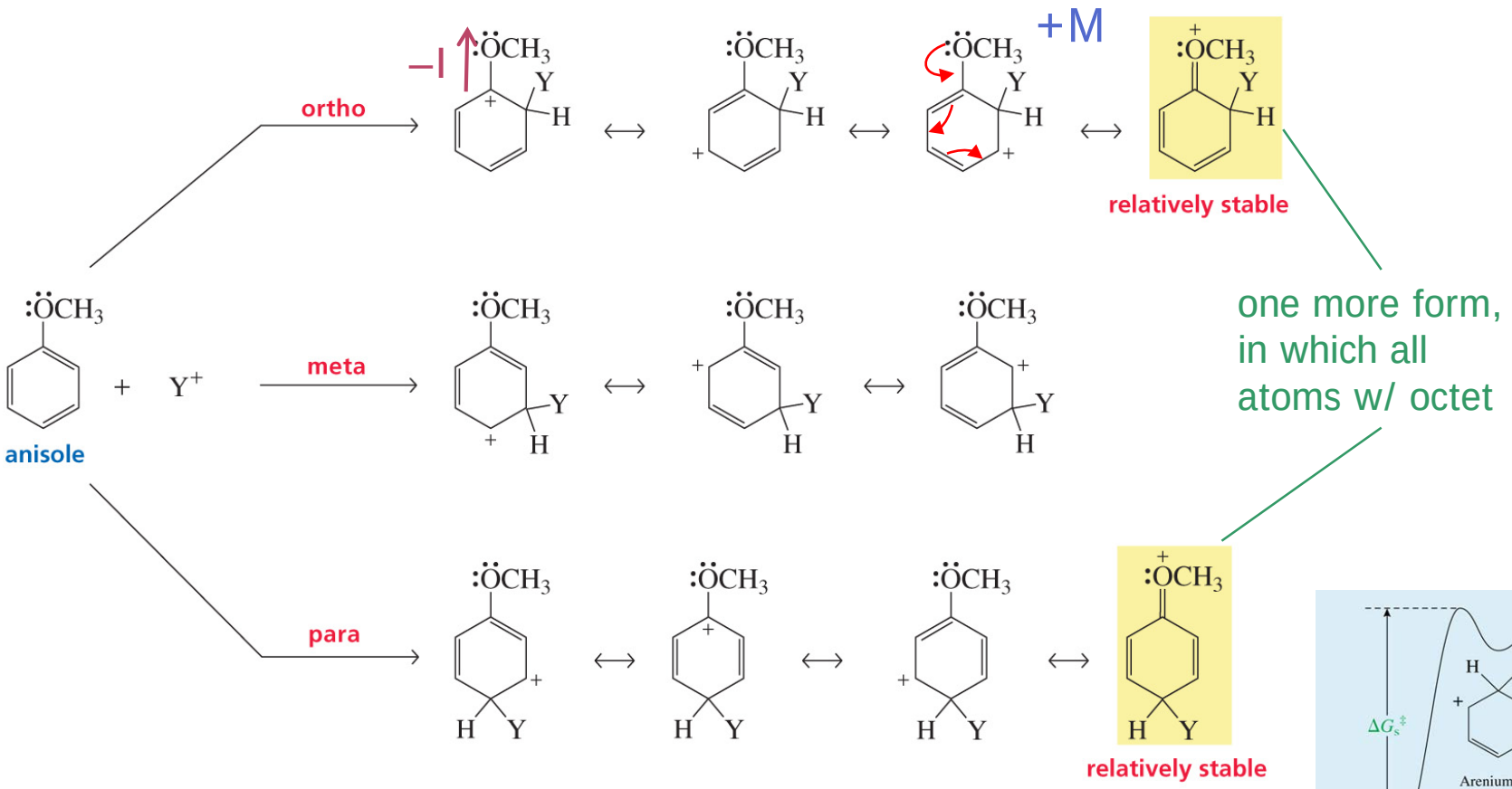
- ortho-para director or meta director

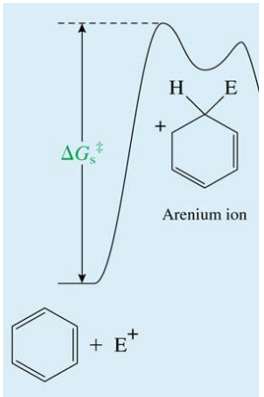


- 3 groups of subs
  - All activating subs [SA, MA, WA] are o-p directors.
  - Halogens are (weakly) deactivating but o-p directors.
  - Other deactivating [MD and SD] subs are m directors.


Activating substituents
Standard of comparison
Deactivating substituents
—NH2
—NHR
—NR2
—OH
—OR
Strongly activating
+M > –I
+M > –I
—NHCR
—OCR
Moderately activating
+M > –I
+M > –I
—R
—Ar
—CH=CHR
Weakly activating
+I (& +M)
+I (& +M)
Ortho/para directing
—H
—F
—Cl
—Br
—I
Weakly deactivating
+M < –I
+M > –I
—CH
—CR
—COR
—COH
—CCl
Moderately deactivating
–M & –I
–I & –M
Meta directing
—C≡N
—SO3H
—NH3
—NH2R
—NHR2
—NR3
—NO2
Strongly deactivating
–M & –I
–I & –M
+M
–I
Cl
Y
H

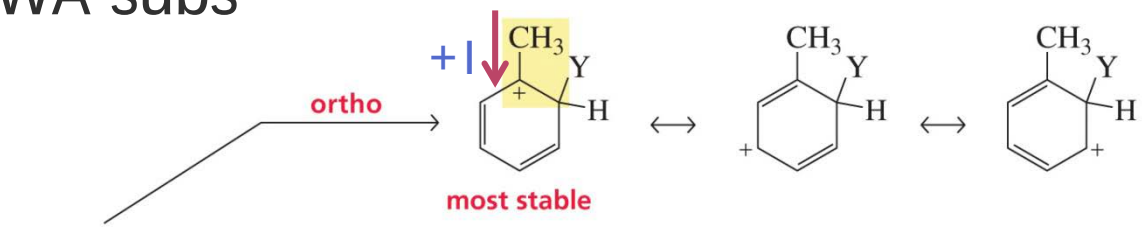
- SA, MA and WD subs ~ +M



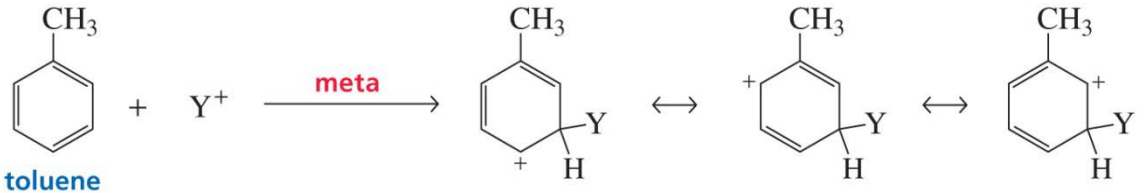


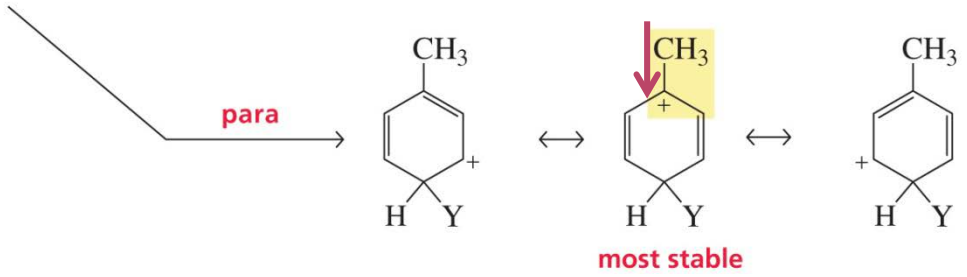
- Subs activates o-p more than m by +M (> –I).

- WA subs

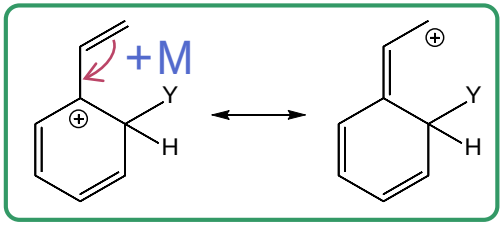


+I ED to (+)



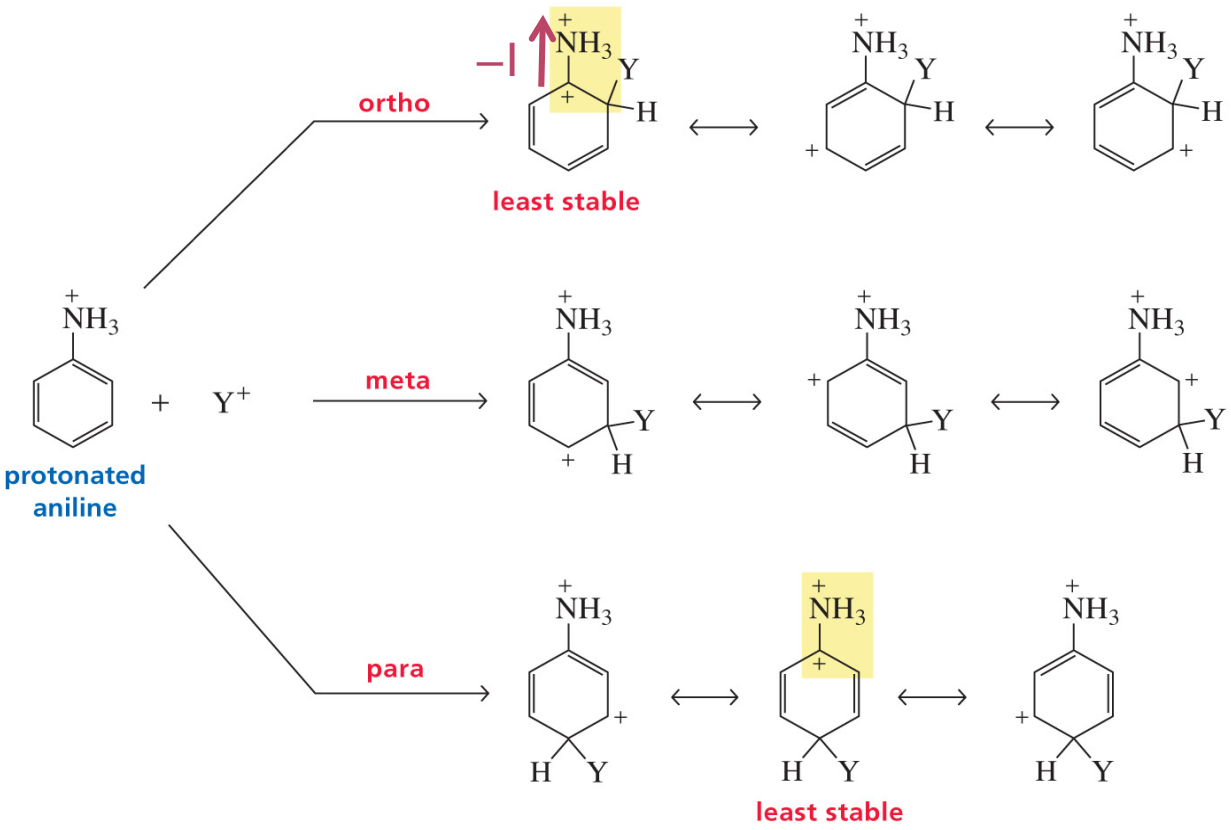


+M ED to (+)

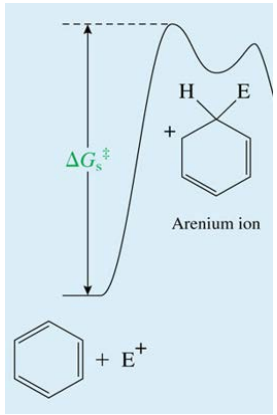


- Subs activates o-p more than m by +I (and +M).
  - in this textbook, R is o-p director by hyperconjugation ED

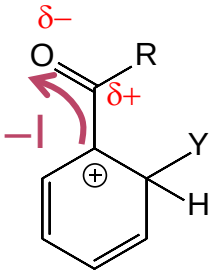
- MD and SD subs



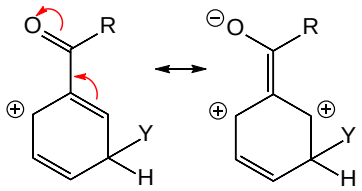
(+) and (+) adjacent



δ+ and (+) adjacent

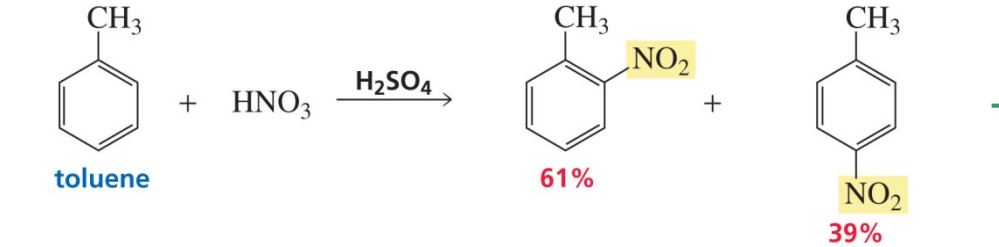


- Subs deactivates m less than o-p by –I (and –M).

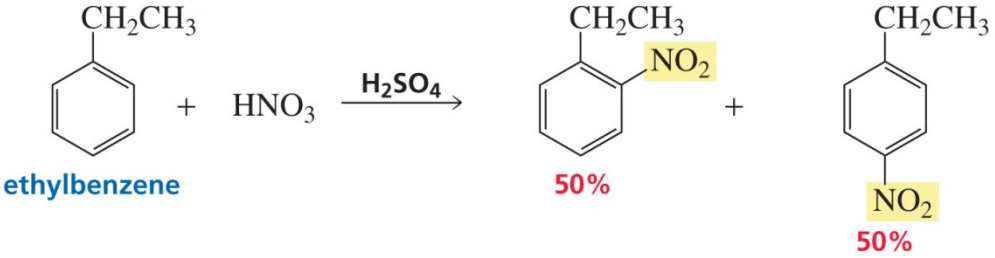


o/p ratio

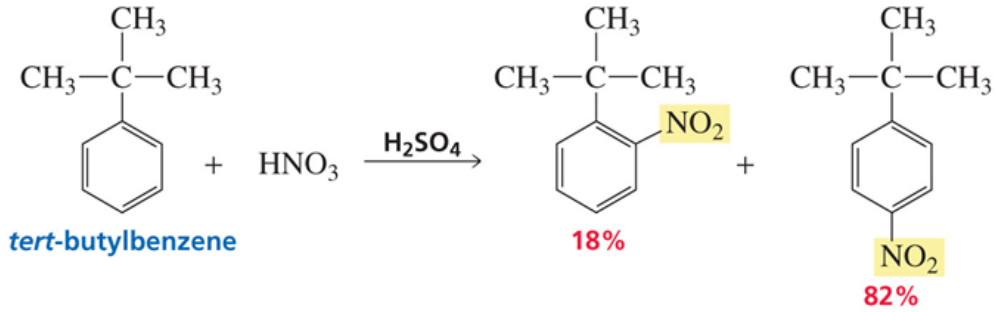
- probability vs steric effect
  - 2 ortho sites vs sterically open para



+ small % of meta



+ small % of meta

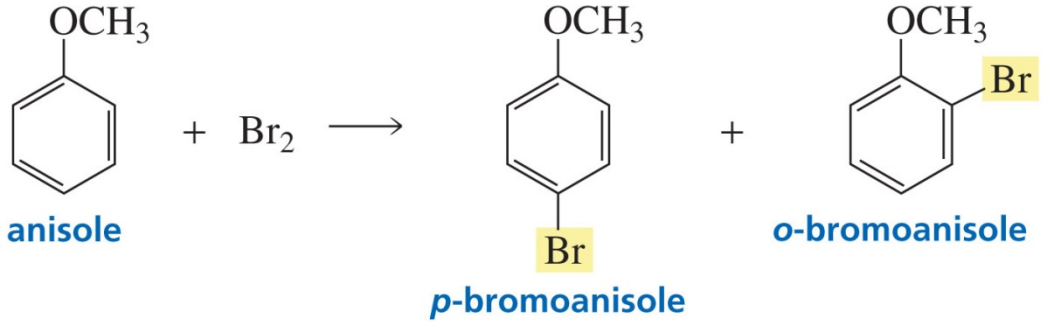


+ small % of meta

- o/m/p isomers are separable!

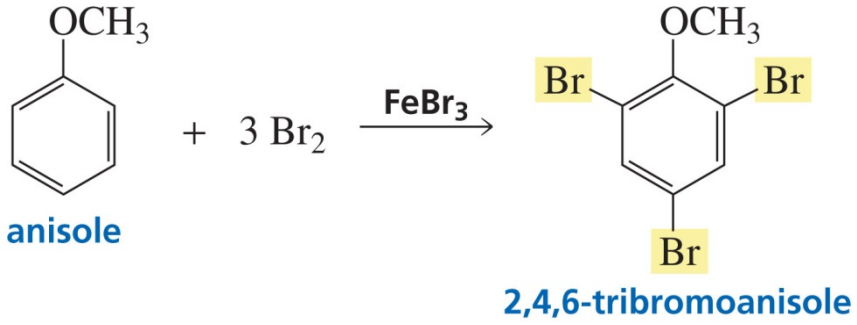
Some special cases

- Halogenation is the fastest (of the 5 rxns).
  - on rings with SA subs, no need of LA



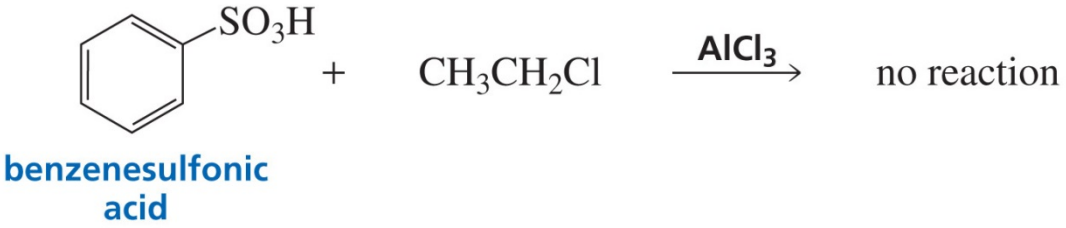
Cl–Cl ~ 58 kcal/mol
Br–Br ~ 54
C–Cl ~ 85
C–Br ~ 70

  - SA with xs Br_2 and LA, multiple subst'n



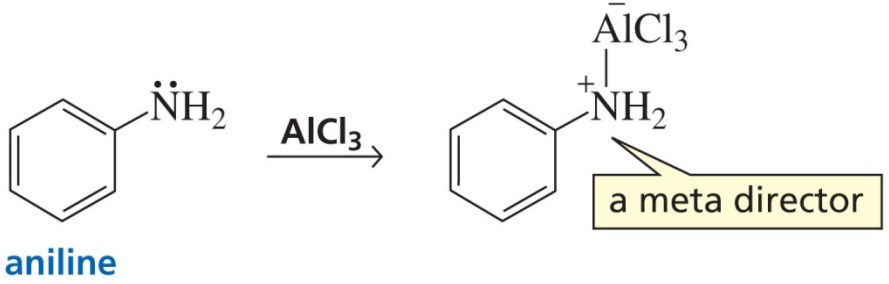
- despite of WD Br
- SA wins over WD.

- Friedel-Crafts rxns are the slowest.
  - no F-C rxn for rings with MD or SD subs [meta directors]



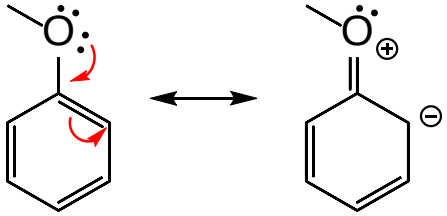
Cl–Cl ~ 58 kcal/mol
Br–Br ~ 54
C–Cl ~ 85
C–Br ~ 70

  - no F-C rxn (with LA) for aniline or N-subst'd aniline



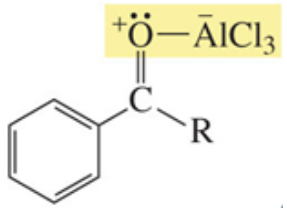
because SA converted to SD

- Friedel-Crafts rxns are the slowest. (cont'd)
  - phenol and anisole undergo F-C rxn

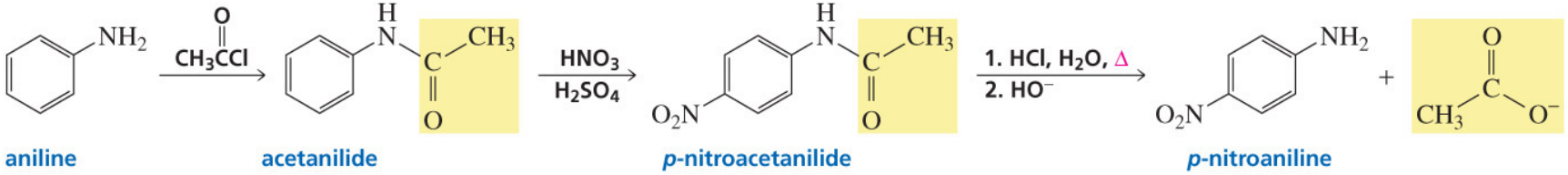


O: weaker B: than N:, and $O^{\delta+}$
→ does not complex with LA

Remember F-C acylation needs > 1 mol LA?
$^{\delta+}C{=}O^{\delta-}$ (by I/M)



- Aniline does not undergo nitration.
  - oxidation by HNO_3 (to $-NO_2$)
  - for nitration, need protection

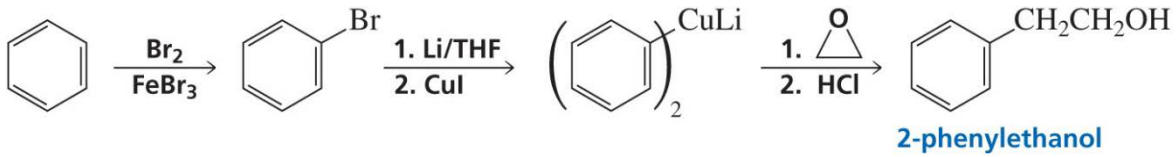


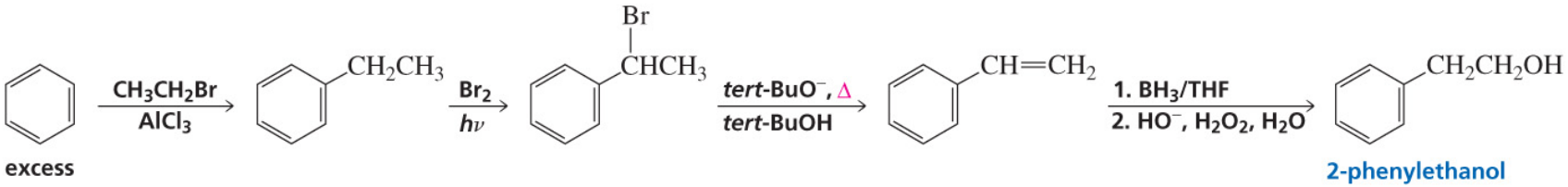
amidation of RCOCl

hydrolysis of amide

Designing a synthesis

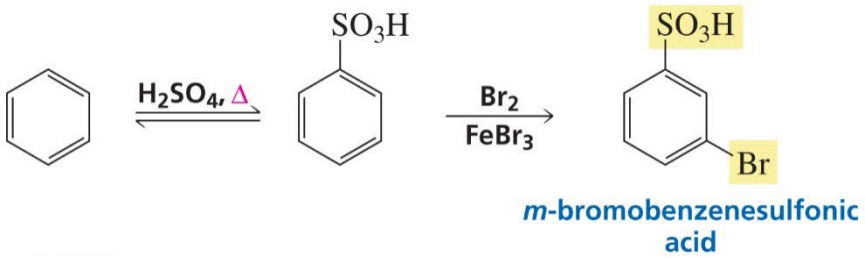
- Between 2 routes



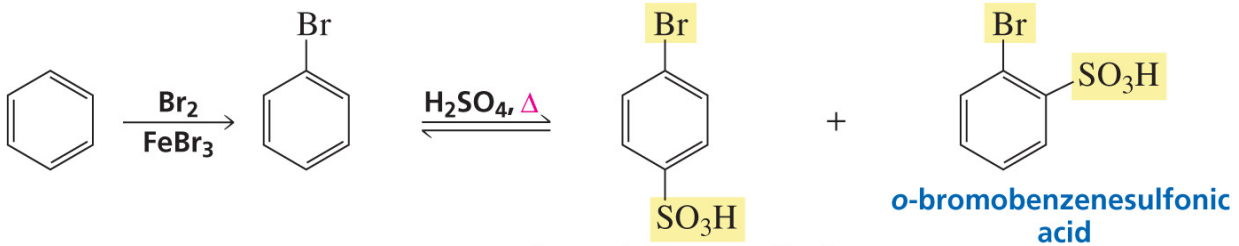


  - considering
    - time and cost
    - # of steps, complexity, yield, and price of reagents
  - preferred route is the upper one
    - multiple alkylation, radical reaction, S_N/E, borane

- For disubst'd bz, order is critical.
  - order of substit'n

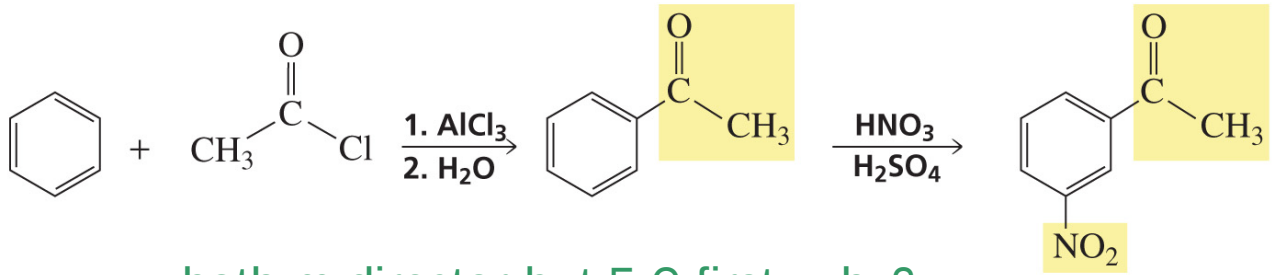


m-bromobenzenesulfonic acid



p-bromobenzenesulfonic acid

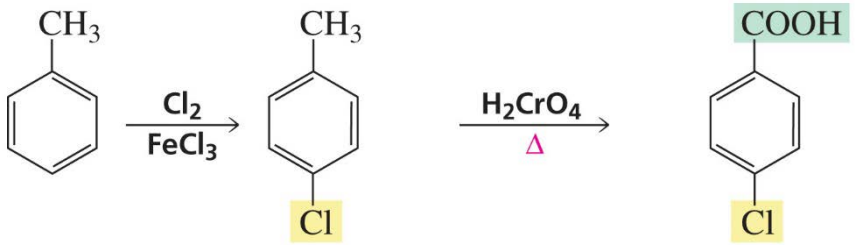
o-bromobenzenesulfonic acid



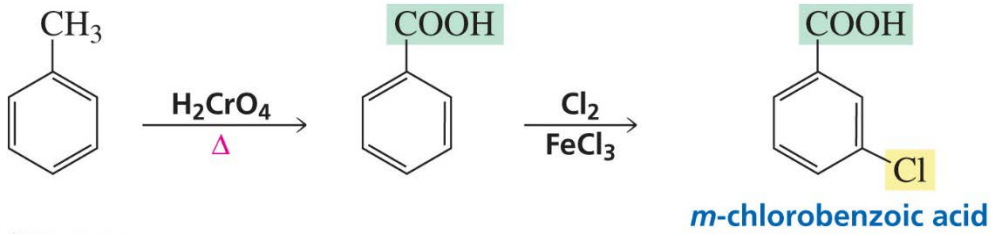
both m director but F-C first. why?

m-nitroacetophenone

- For disubst'd bz, order is critical. (cont'd)
  - order of modification

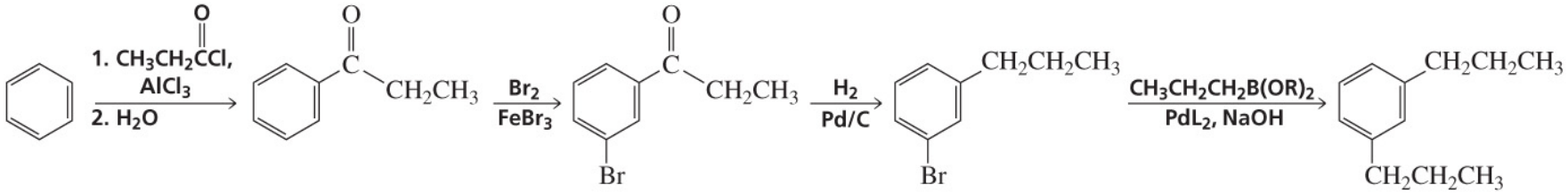


p-chlorobenzoic acid



m-chlorobenzoic acid

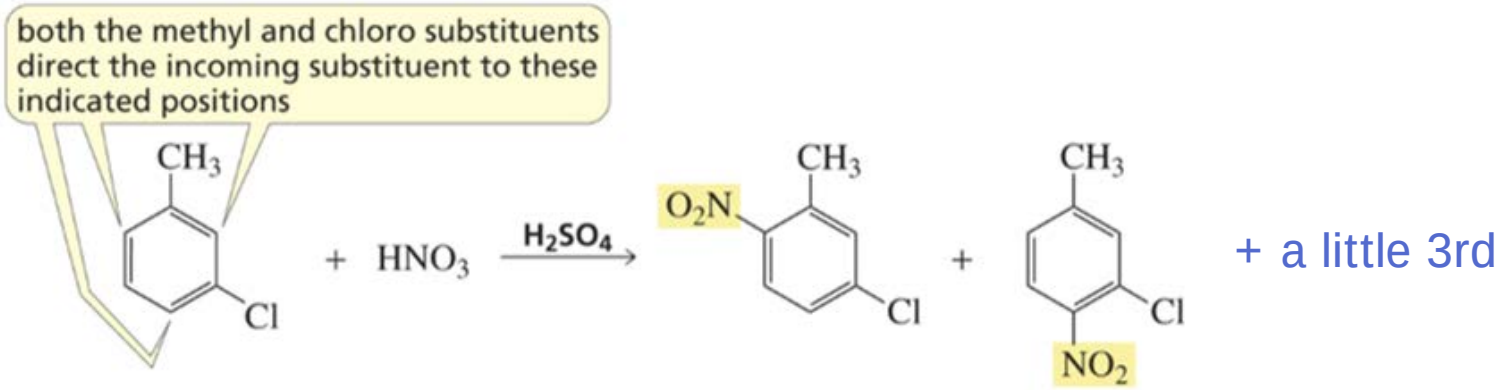
- sometimes, no choice



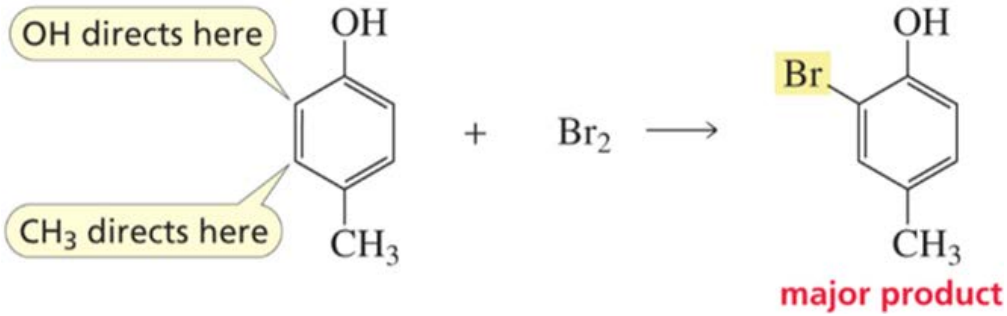
m-dipropylbenzene

Third substitution

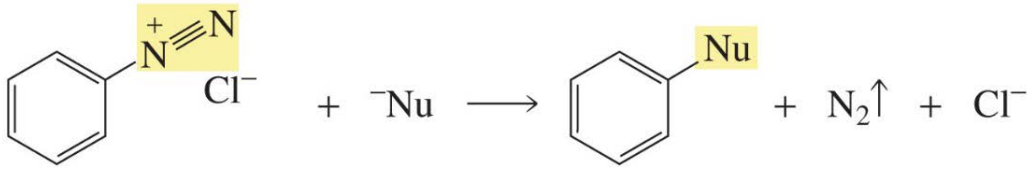
- when directions coincide



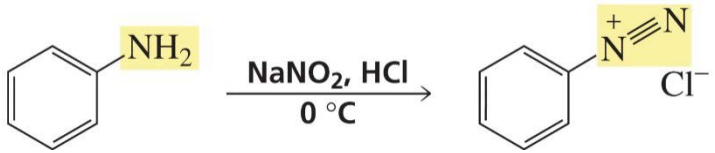
- when directions conflict
  - SA > MA > --- > SD



Substit'n using diazonium salt



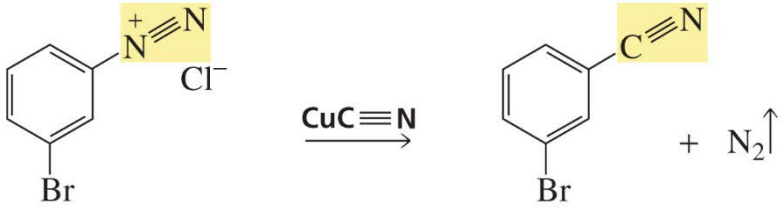
benzenediazonium chloride



an arenediazonium salt
~ prepared *in situ*
← HNO_2 and ArN_2Cl unstable

- a nucleophilic substitution [S_N]!! no S_N on aryl or vinyl. p472
  - possible because of very reactive diazonium ion
    - very stable and good-leaving N_2
  - not clear whether S_N1 or S_N2

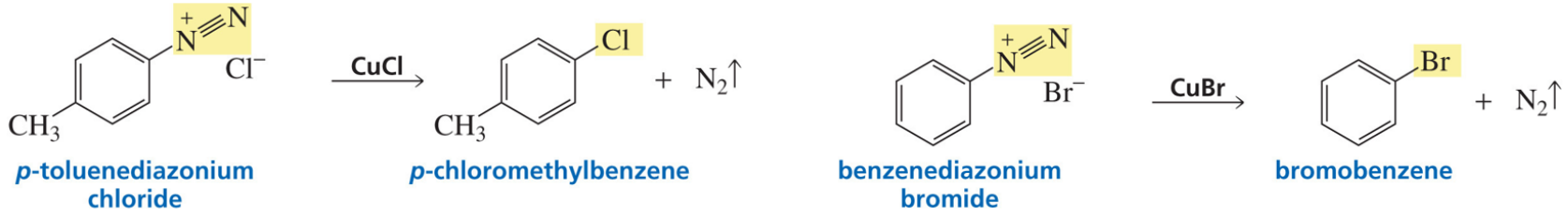
- Sandmeyer reaction
  - diazonium salt + Cu(I) salt



m-bromobenzenediazonium chloride

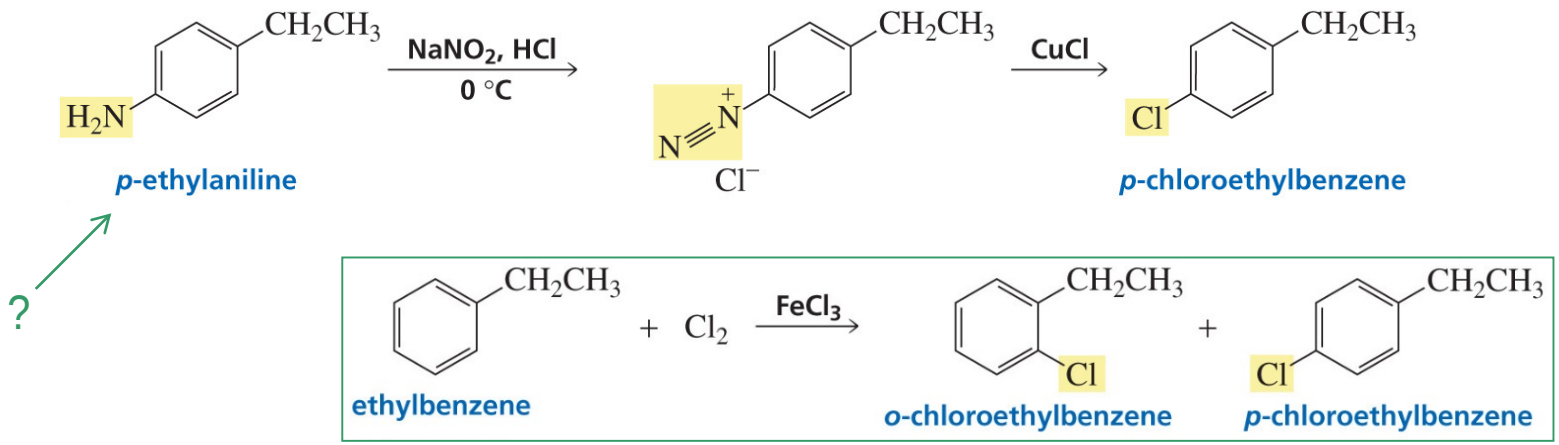
m-bromobenzonitrile

Sandmeyer reaction (cont'd)



p-toluenediazonium chloride | *p*-chloromethylbenzene | benzenediazonium bromide | bromobenzene

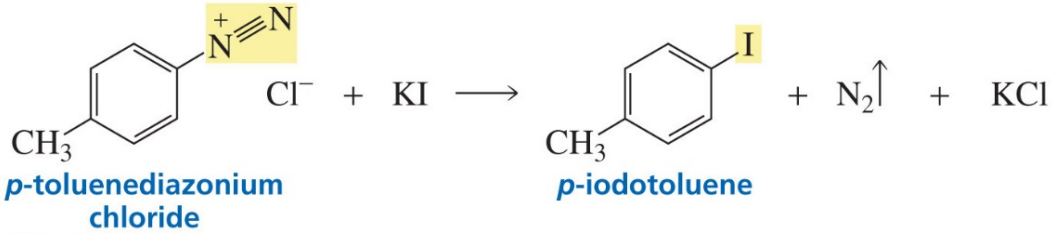
- mechanism not clear; may involves arene radical (by Cu(I))
  ← KCl or KBr doesn't work.
- useful for only product



p-ethylaniline | *p*-chloroethylbenzene

ethylbenzene | *o*-chloroethylbenzene | *p*-chloroethylbenzene

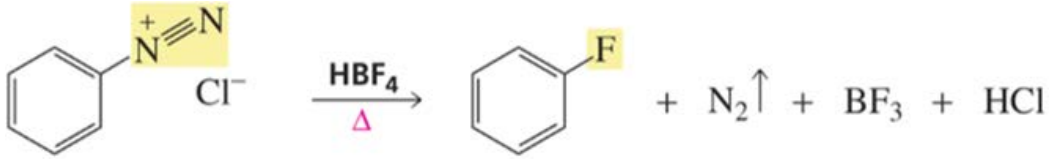
- iodination



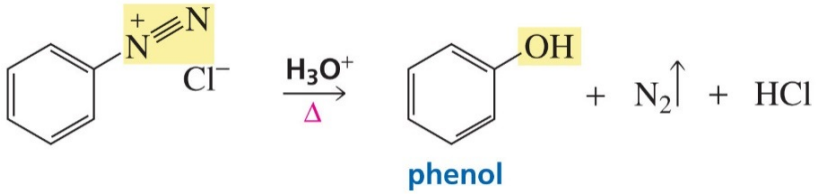
  - KI works.

- fluorination ~ Schiemann reaction

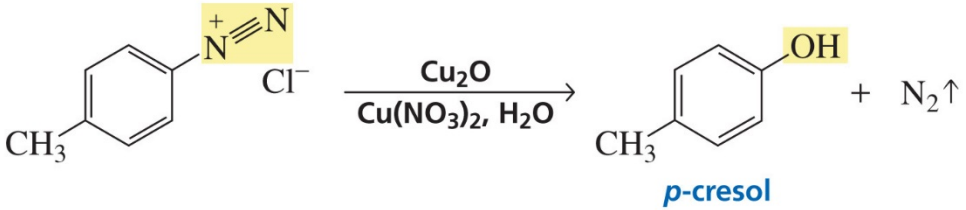
monofluorobz enabled



- phenol synthesis



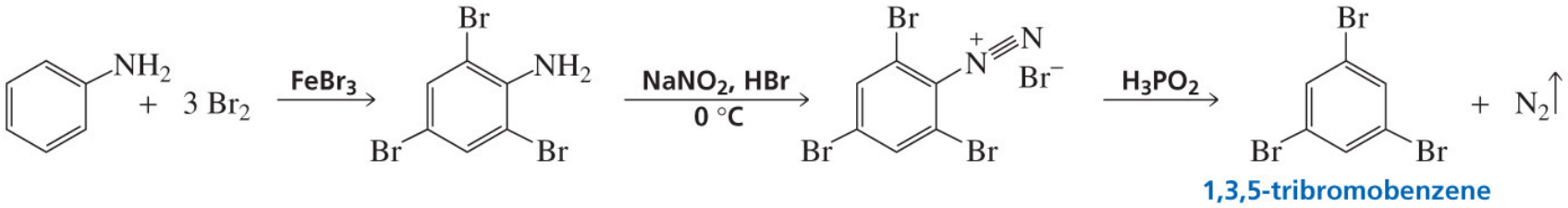
acidic aq soln of ArN_2Cl
just warmed up



use of Cu(I)O + Cu(II)NO_3
→ better yield

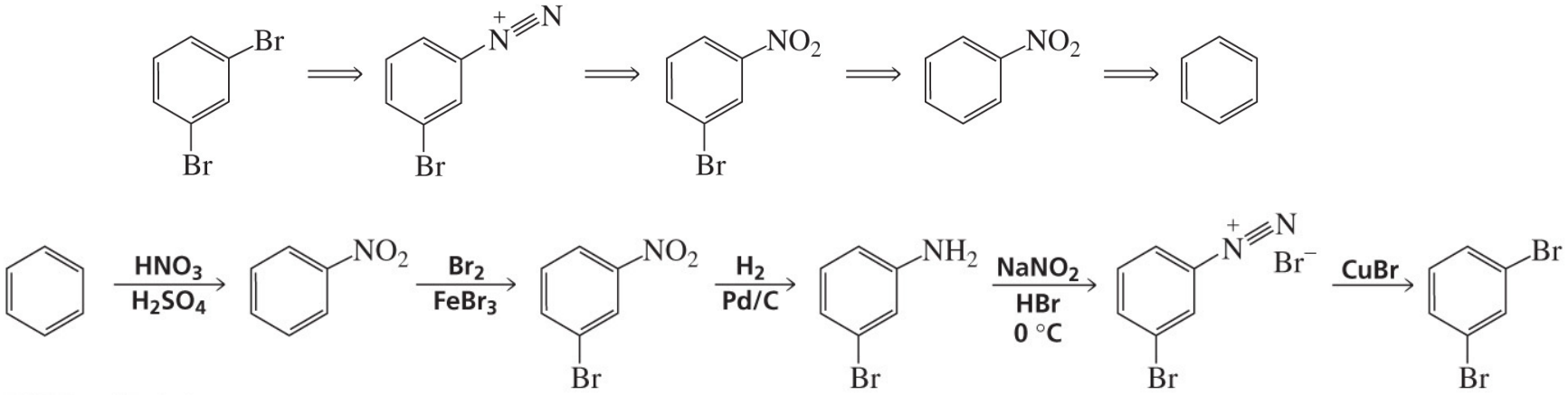
a Sandmeyer reaction

- replace with H

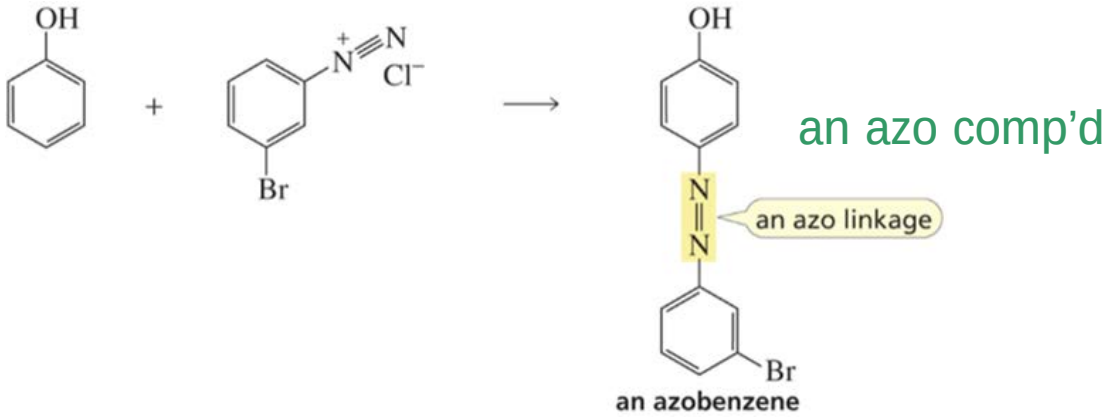


  - with H_3PO_2 or $NaBH_4$
  - useful for directing-and-removing

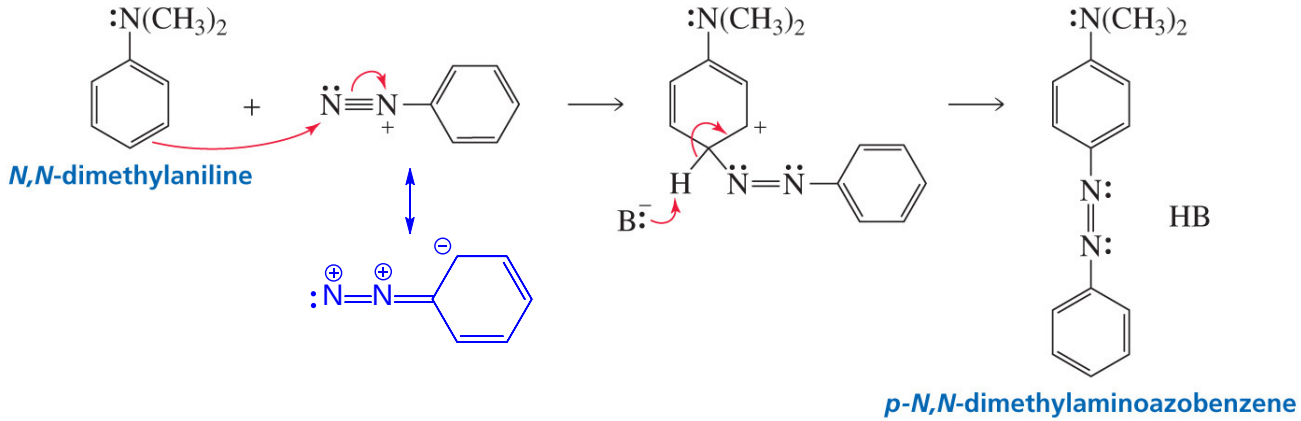
- retrosynthetic



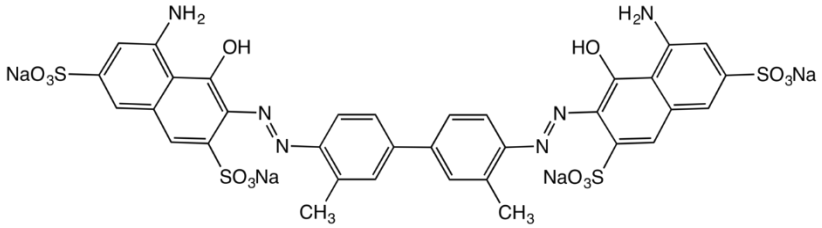
Ar-N_2^+ as E^+ → azo comp'd



- an e-philic aromatic substit'n
  - Ar-N_2^+ unstable → rxn at low Temp → only for SA-subst'd bz
  - bulky E+ → on para; ortho when p occupied

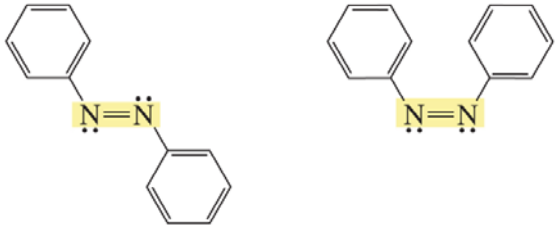


- Aromatic azo comp'ds are dyes.
  - 'azo dye'

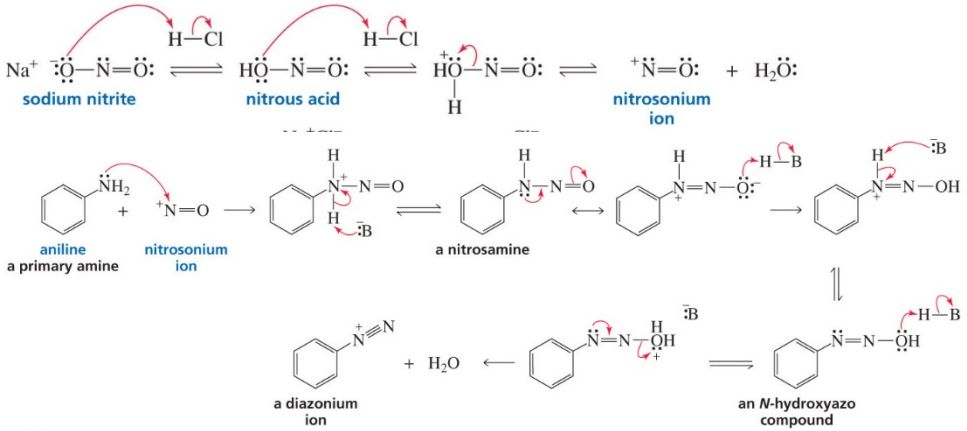


dye [染料] vs pigment［顔料］

- azobenzenes in cis and trans forms
  - trans more stable ← steric



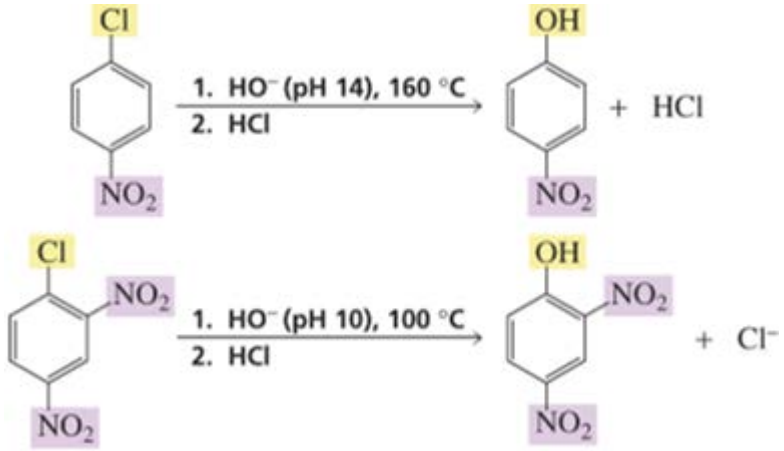
- formation of diazonium ion

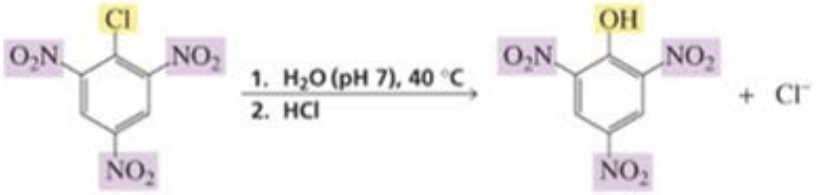


  - unstable ~ prepared in situ and used immediately
    - from $NaNO_2$ + HCl

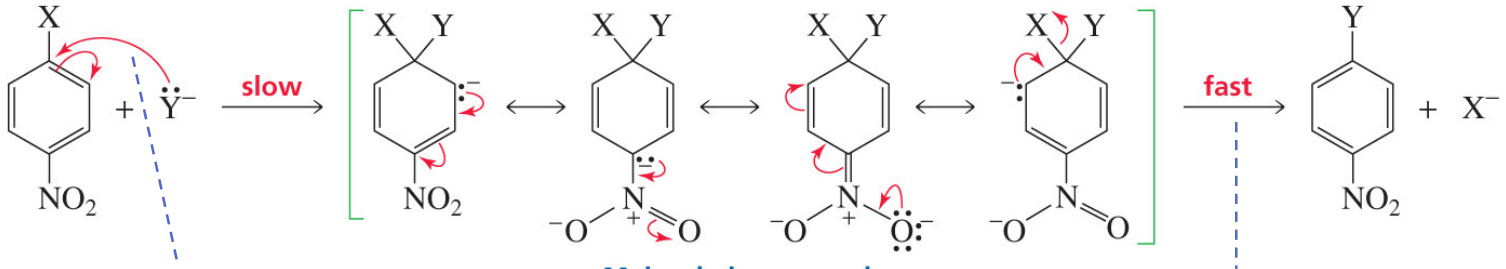
S_NAr reaction

- nucleophilic aromatic substitution
  - only when strong EWG [SD] present (at o and/or p)





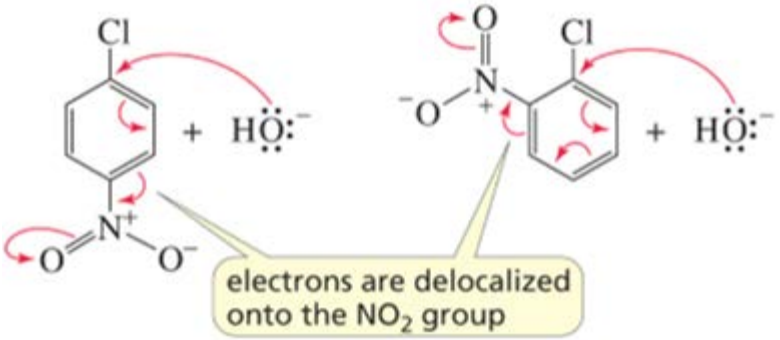
- mechanism ~ S_NAr ~ addition-elimination not S_N1 or S_N2



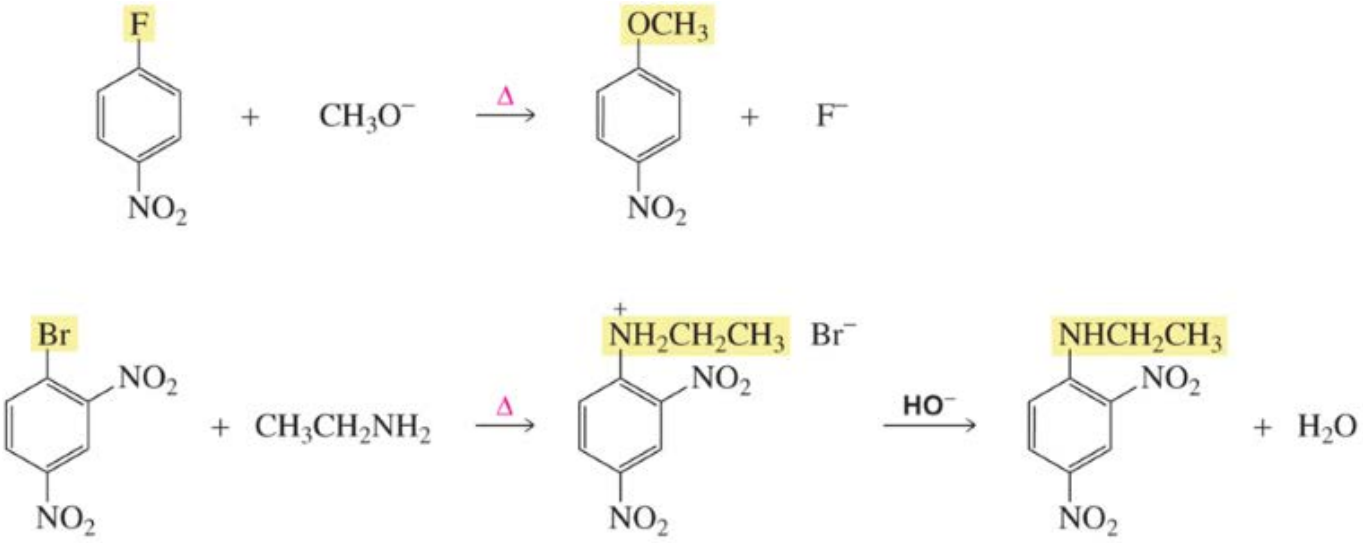
approaches
nearly ⊥ to ring

Weaker B: betw X/Y leaves.
→ Y should be a stronger B:.

- EWG must be at o or p position to X.
  - to delocalize the e of Nu: (and to stabilize interm)

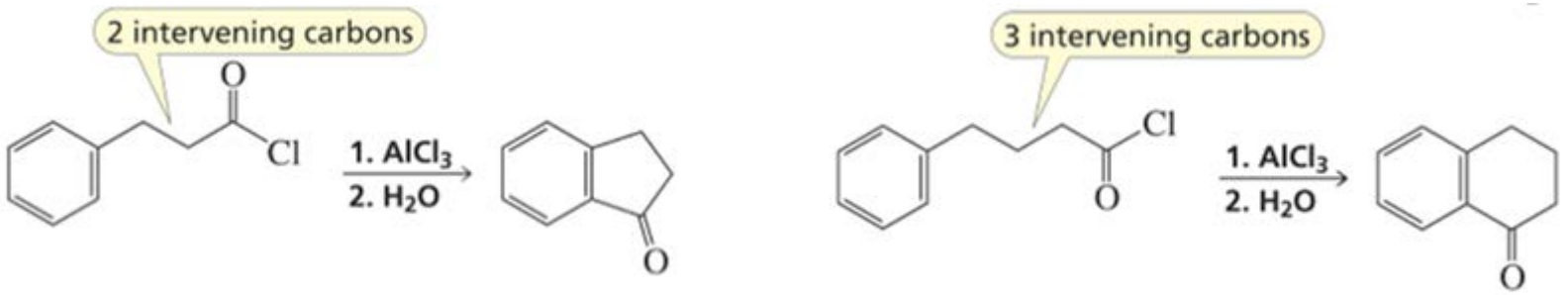


- The incoming should be a stronger B: than the leaving.



Intramol rxn → cyclization

- intramol F-C acylation → cyclic ketone



- intramol Fischer esterific'n → lactone

- intramol Williamson synthesis → cyclic ether